[Prophylactic value of vitamin C in acute respiratory tract infections in schoolchildren].

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Minor further editing by Harri Hemilä
harri.hemila@helsinki.fi
https://www.mv.helsinki.fi/home/hemila
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https://www.mv.helsinki.fi/home/hemila/CC.htm (Cochrane review)
https://www.mv.helsinki.fi/home/hemila/CC (Cochrane review references)

This translation is located at:
version 2020-6-9

The Spanish text:

Note of the translator:
In Figure 1, there is a typo in the Spanish: it says “48 days” instead of “84 days.” 84 is clearly the right number, because the study lasted 12 weeks, which equals 84 days.
Also, on page 3 of Vitamin C – Eng.doc, the first paragraph after the subtitle “RESULTS,” the “X” should be X with a line ON TOP of it, which stands for the arithmetic mean. The same is true of the “X” in Table 1. I couldn’t find any way to type that symbol.

Note of Harri Hemilä:
In the original abstract, the authors describe the duration of colds as 3.4±0.45 SD and 4.5±0.43 SD in vitamin C and placebo groups. The variation measure in the original text must be SE, which corresponds to 3.4±2.77 SD and 4.5±2.92 SD. These lead to P(1-tail)=0.04 which is consistent with the authors calculation. Therefore the original SD term is corrected here to SE.
THE VALUE OF VITAMIN C IN THE PREVENTION OF ACUTE RESPIRATORY INFECTIONS IN SCHOOLCHILDREN

DR. ALDO BANCALARI M., DR. CLAUDIO SEGUEL C., FLOR NEIRA C., INES RUIZ A. AND CARLOS CALVO M. (BIOCHEMIST)

The value of 2 g per day of vitamin C for 12 weeks in preventing acute respiratory infection (ARI) was evaluated during wintertime in 62 schoolchildren (10 to 12 years old), using double-blind research techniques. In the placebo group (n=30), 46 episodes of ARI were detected, as compared with 38 episodes of ARI in the vitamin C group (n=32). The vitamin C group evidenced a significant decrease (p<0.05) in the duration of ARI (3.4 days ± 0.45 SE), as compared with the placebo group (4.5 days ± 0.43 SE). In general, children treated with vitamin C had 37% less days sick with ARI than the placebo group. The common cold was the most frequent cause of ARI in both groups. The basal level of ascorbic acid in plasma was similar in both groups and more than doubled in the group treated with vitamin C. Vitamin C was subjected to both clinical examination and laboratory tests, to check for side effects, and none was found. Results suggest that vitamin C does not prevent ARI in children, but does shorten its duration. (Key words: Upper respiratory infections; Ascorbic acid; Primary prevention.)

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Pediatric Service, Coronel Hospital
Concepción-Arauco Health service, 8th Region, and Department of Applied Biochemistry.
School of Pharmaceutical Chemistry and Biochemistry, University of Concepción, Chile.

Vitamin C has been utilized widely in the prevention and treatment of acute respiratory infections (ARI), with or without doctors’ prescriptions. Its use increased with the 1970 publication of Linus Pauling’s book Vitamin C and the Common Cold, which contends that high doses of vitamin C, administered daily, prevent the common cold and other acute respiratory infections. Pauling suggests a daily dosage of 1 to 3 g of vitamin C, in order to achieve the desired effect. He also revealed that in 1970-71 in the United States, 1 the common cold resulted in lost work worth 15 million dollars annually.

In Chile, children are often absent from school during the winter months due to ARI, especially those from families in the middle- and low-income classes.

The purpose of this article is to evaluate the usefulness of vitamin C as a means of preventing ARI in a group of schoolchildren, and to investigate this vitamin’s possible side effects.
MATERIALS AND METHODS

Sixty-two elementary school students in two different grades, ages 10 to 12 and predominantly girls, from Educational Unit D No. 675 in the city of Coronel, were studied during the winter months of June through September, 1981. (Table 1)

The 62 students were divided into two random groups: the vitamin C group (n=32) and the placebo group (n=30). The vitamin C tablets (2 g per day) and the placebo tablets were identical in color, taste, size and consistency, and were marked with codes understood only by staff members in the Department of Applied Biochemistry of the University of Concepción. Like the children, those who collected the data did not know who was taking vitamin C and who was taking the placebo (i.e., it was a double-blind study).

The vitamin C and the placebo were administered to the children by one of the authors of this article, for a period of 12 weeks. The vitamin C utilized was Cebion 2000 (graciously contributed by Merck laboratories) and the placebo consisted of glucose, prepared by the Department of Applied Biochemistry, School of Pharmaceutical Chemistry and Biochemistry of the University of Concepción.

<table>
<thead>
<tr>
<th>Group</th>
<th>Children n</th>
<th>Sex</th>
<th>X age (years)</th>
<th>Nutritional state (weight/height)*</th>
</tr>
</thead>
<tbody>
<tr>
<td>Students taking Vit. C</td>
<td>32</td>
<td>11 21</td>
<td>11.3</td>
<td>2 &lt; P₁₀</td>
</tr>
<tr>
<td>Students taking placebo</td>
<td>30</td>
<td>12 18</td>
<td>11.8</td>
<td>3 &lt; P₁₀</td>
</tr>
</tbody>
</table>

*H. Stuart percentiles
M = masculine  F = feminine

On Saturdays and Sundays, each child was supplied with the vitamin C or placebo tablets, following conversations with the parents or guardians, in order to ensure that the tablets were ingested properly.

The children were examined for acute respiratory infection three times a week, and their temperatures were taken orally when any respiratory symptom was detected. The duration of each acute respiratory episode was determined in line with previously established guidelines. When a child was absent from school, one of the authors went to the student’s home to find out the reason. If the child was sick, the evolution of the illness was monitored until he or she was completely well. With the goal of researching possible side effects, testing was done for blood glucose, glucosuria, urinary pH, ketonuria, proteinuria, hematuria, and plasma electrolytes. Furthermore, medical histories were maintained, in order to find any gastrointestinal effects. Spectrophotometric analysis of ascorbic acid levels were taken before, during (days 20, 50 and 80), and 48 hours after the treatment concluded.²

This project was carried out with the written permission of the children’s parents and/or guardians, and of Educational Unit D No. 675.
RESULTS

During the 12 weeks of the study, there were 46 ARI episodes detected in the control group and 38 episodes in the vitamin C group (Figure 1). Moreover, in the group that received the vitamin C there was a significant decrease (p<0.05) in the duration of each ARI episode ($X \pm 3.4$ days ± 0.45 SE), compared with the control group (4.5 days ± 0.43 SE) (Figure 2).

**Figure 1.** Number of episodes of acute respiratory infection in schoolchildren who received vitamin C or placebos for 48 days (not copied here)

**Figure 2.** Average length of each acute respiratory infection in schoolchildren who received vitamin C or placebo tablets (not copied here)


An equal number of children in both groups analyzed had more than one ARI episode. Nonetheless, in the group receiving supplemental vitamin C, the number of recurring episodes in the time period studied was significantly less (p<0.02) than in the group that received the placebos (Table 2). Of the 32 children who received vitamin C, 11 (34.3%) did not have a single episode of ARI during the 84 days of the study, and in the group of students receiving placebos, 9 (30.0%) did not have any ARI episode (Table 3).

**Table 2.** Effect of Vitamin C vs. placebo on the recurrence of acute respiratory infections during the period under study

<table>
<thead>
<tr>
<th>Group</th>
<th>Children with more than one episode of ARI</th>
<th>$X$ and SD of recurrent ARI</th>
</tr>
</thead>
<tbody>
<tr>
<td>Vitamin C (n = 32)</td>
<td>11</td>
<td>2.36 ± 0.16</td>
</tr>
<tr>
<td>Placebo (n = 30)</td>
<td>11</td>
<td>3.09 ± 0.84</td>
</tr>
<tr>
<td><strong>p &lt; 0.02</strong></td>
<td></td>
<td></td>
</tr>
</tbody>
</table>

**Table 3.** Effect of Vitamin C vs. placebo on the number of acute respiratory infections during the period under study

<table>
<thead>
<tr>
<th>Group</th>
<th>Number of subjects with no ARI episodes</th>
<th>%</th>
</tr>
</thead>
<tbody>
<tr>
<td>Vitamin C (n = 32)</td>
<td>11</td>
<td>34.3</td>
</tr>
<tr>
<td>Placebo (n = 30)</td>
<td>9</td>
<td>30.0</td>
</tr>
</tbody>
</table>
The most frequent type of ARI diagnosed in both grades was the common cold (Figure 3), but its average duration was significantly less (p < 0.05) in the children taking vitamin C (Figure 4).

A total of 131 sick days were detected in the children who received vitamin C and there were 208 sick days among the children in the placebo group, which signifies 37% less sick days in the group of children receiving vitamin C (Table 4). Basal ascorbic acid levels were within normal ranges for both groups, and no possible case of scurvy was encountered. Average basal ascorbic acid levels, measured in mg/l, for the children treated with vitamin C was $10.8 \pm 3.5$ SD. This value rose to almost double within 20 days, reached its highest level at 50 days ($24.7 \pm 5.3$ SD) and maintained a similar level at 80 days. Ascorbic acid levels reached its basal level 48 hours after the administration of vitamin C ended. No changes were observed in ascorbic acid deficiency in the placebo group (Figure 5).

**Figure 3.** Acute respiratory infections diagnosed in schoolchildren who received vitamin C or placebos for 84 days (not copied here)

**Figure 4.** Average duration of each episode of common cold in schoolchildren who received Vitamin C or placebos (not copied here)


**Table 4.** The number of days the schoolchildren taking vitamin C or placebo had ARI (during the 84 days of the study)

<table>
<thead>
<tr>
<th>Group</th>
<th>Schoolchildren N</th>
<th>Number of days sick</th>
</tr>
</thead>
<tbody>
<tr>
<td>Vitamin C</td>
<td>32</td>
<td>131*</td>
</tr>
<tr>
<td>Placebo</td>
<td>30</td>
<td>208</td>
</tr>
</tbody>
</table>

* –37 %

Neither the medical histories conducted by the authors, nor the laboratory tests revealed any side effects of vitamin C (Table 5). The ranges of blood glucose, plasma electrolytes and urinary pH remained within normal limits throughout the study period.
Figure 5. Ascorbic acid levels before, during and after the period of taking vitamin C, compared with the placebo group (not copied here)

see https://www.mv.helsinki.fi/home/hemila/CC/Bancalari_1984_bm.pdf

None of the schoolchildren in the two grades analyzed were excluded from testing.

In the statistical analysis, the unmatched Student t-test was used.3

Table 5. Laboratory tests in schoolchildren during the administration of vitamin C

<table>
<thead>
<tr>
<th>Tests*</th>
<th>Basal</th>
<th>20 days</th>
<th>50 days</th>
<th>80 days</th>
</tr>
</thead>
<tbody>
<tr>
<td>Blood glucose (g/dl)</td>
<td>0.99</td>
<td>1.01</td>
<td>1.07</td>
<td>1.05</td>
</tr>
<tr>
<td>Na* (mmol/l)</td>
<td>142</td>
<td>141</td>
<td>137</td>
<td>138</td>
</tr>
<tr>
<td>K* (mmol/l)</td>
<td>4.6</td>
<td>4.6</td>
<td>4.4</td>
<td>4.3</td>
</tr>
<tr>
<td>Urinary pH</td>
<td>6.3</td>
<td>6.2</td>
<td>6.2</td>
<td>6.3</td>
</tr>
<tr>
<td>Proteinuria</td>
<td>(-)</td>
<td>(-)</td>
<td>(-)</td>
<td>(-)</td>
</tr>
<tr>
<td>Ketonuria</td>
<td>(-)</td>
<td>(-)</td>
<td>(-)</td>
<td>(-)</td>
</tr>
<tr>
<td>Hematuria</td>
<td>(-)</td>
<td>(-)</td>
<td>(-)</td>
<td>(-)</td>
</tr>
</tbody>
</table>

* Average values

Basal: 2 days before the administration of vitamin C
DISCUSSION

This study did not demonstrate that the daily administration of vitamin C has a prophylactic effect, even though the children who received vitamin C supplements had a lower incidence of respiratory episodes during the period studied. Indeed, the length of each ARI episode was shorter among the schoolchildren treated with vitamin C, compared with those who received placebos. It is clear that episodes of the two types of ARI found most frequently in both groups of children, the common cold and acute pharyngitis, were much shorter in the children who received vitamin C.

Some studies have demonstrated that vitamin C, administered on a preventive basis and/or therapeutically, limited the severity and duration of the common cold.\textsuperscript{4, 5} The work of Charleston and Clegg\textsuperscript{6} and Anderson \textit{et al}\textsuperscript{7} show significant differences in the incidence and duration of the common cold in individuals treated with high doses of ascorbic acid, in comparison with those receiving placebos.

This beneficial action of vitamin C must be because the levels of ascorbic acid within leukocytes are kept from dropping,\textsuperscript{8} given that polymorphonuclear leukocytes’ bactericidal activity seems to depend on an adequate supply of ascorbic acid, which stimulates various biochemical mechanisms, including the hexode monophosphate shunt.\textsuperscript{9} Furthermore, aspirin – which is widely utilized as symptomatic treatment for ARI – facilitates the leukocytes’ absorption of ascorbic acid and increases ascorbic acid’s presence in tissues during the common cold,\textsuperscript{10} thereby inhibiting the synthesis of prostaglandines and decreasing the inflammatory response.\textsuperscript{11, 12} This points up the importance of controlling the clinical symptoms of the common cold and other upper respiratory illnesses, by boosting the normal defense mechanisms through the restoration of ascorbic acid concentrations in the tissues.

A normal diet contains at least 30 mg. of vitamin C,\textsuperscript{13} which is sufficient for the maintenance of normal concentrations of ascorbic acid in the leukocytes and plasma of healthy people. However, the ascorbic acid of polymorphonuclear leukocytes quickly diminishes during the course of a common cold and spontaneously returns to normal when the symptoms disappear, on about the fifth day.\textsuperscript{14}

Some published research\textsuperscript{15, 16} has found no difference in the incidence, duration or severity of the common cold in individuals treated with vitamin C, compared with those taking placebos. Cowan \textit{et al}\textsuperscript{17} did not find significant differences in the frequency, duration or severity of the common cold in 400 students who received 200 mg. of vitamin C daily for seven months, compared with the control group. These unfavorable results of the administration of vitamin C for the common cold could be related to the small amounts of
vitamin C utilized, since it has been demonstrated that at least 6 gr. of vitamin C\textsuperscript{14} prevents the decrease of ascorbate in leukocytes. This fact could also explain why our study did not observe vitamin C’s preventive effect in ARI, because we only used 2 gr. daily.

On the other hand, we would like to point out that although 11 children in each group developed more than one ARI during the 12 weeks of the study, the children treated with vitamin C had a significantly lower rate of recurrent respiratory episodes, and this suggests a certain preventive effect in this group. We also found less sick days in the group of children treated with vitamin C, compared with the schoolchildren taking the placebo, and this is in accordance with several other published studies\textsuperscript{7, 18}.

Numerous studies have indicated adverse reactions of vitamin C in high dosages. They have described the possible development of kidney stones, acidification of pH in the urine and blood, changes in bone metabolism in the presence of hyperglycemia, glucosuria, hemolysis in patients with glucose-6-phosphatase dehydrogenase deficiency, destruction of vitamin B-12, gastrointestinal changes, etc.\textsuperscript{1, 9} However, Dykes and Meier,\textsuperscript{20} Körner and Weler\textsuperscript{21} – who have been especially interested in the possible toxic effects of ascorbic acid in high doses – agree that to date there are not enough valid data indicating any significant harmful effect on human health. Moreover, other published research found no adverse effects of vitamin C, even in dosages greater than 3-5 g per day.\textsuperscript{22, 23} Recently, it has been shown that the ingestion of 8-10 g daily leads to a very slight decrease in blood pH,\textsuperscript{24} which would cause other conditions.

This study did not reveal any side effect of vitamin C at the administered dosage (2 g per day) in children who weighed between 27.5 and 33 kg., and no gastrointestinal or other changes were detected. The results of the lab tests did not vary during the periods under study.

The basal levels of ascorbic acid in the children studied were within normal ranges.\textsuperscript{2, 5} The children who received vitamin C supplements reached their highest average level of ascorbic acid at 50 days. Two days after the vitamin C supplementation ended, the average ascorbic acid level was slightly lower than basal levels (Figure 5). We did not carry out subsequent long-term tests of ascorbic acid levels, because it had already been proven that administering vitamin C in doses of 1-2 g per day does not cause significant decreases in those levels.\textsuperscript{26}

Furthermore, we consider it important to note that the nutritional status and socioeconomic levels of the two groups of children tested were similar. They all lived in an urban setting, in a fairly closed community, and all attended the same school. This allows us to assume that the epidemiological conditions were equal for the majority of the children. These facts offer even greater support for the results obtained.
This clinical experiment does not resolve all the questions related to this issue. But the evidence that ARI episodes among the children treated with vitamin C were shorter in duration suggests that ascorbic acid does have some pharmacological effect. For that reason, we feel that it is necessary to carry out more studies, in order to clarify vitamin C’s exact mechanism of action. This would provide a more solid basis for proscribing this vitamin for the prevention of acute respiratory infections in children.

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