Doctors Need To Know About

Ascorbic Acid and Common Cold

Part II

By LINUS PAULING, NOBELIST

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This concludes the examination of published studies of vitamin C and the common cold by Linus Pauling, Ph.D., which MEDICAL TRIBUNE is publishing because the information is important to physicians, and the paper was rejected by the Journal of American Medical Association even after Dr. Pauling twice made revisions to meet the suggestions of its referees.

DAHLBERG, ENGEL, AND RYDIN

Dykes and Meier mention the double-blind study by Dahlberg, Engel, and Rydin[16] of 2,525 Swedish soldiers in a camp in northern Sweden during 90 days in 1941, and say that no differences were found in either the incidence or the duration of colds. The ascorbic-acid subjects (1266) received an average of 90 mg per day, and the control subjects (1259) received a placebo: Examination of the tables shows that the incidence of colds in the ascorbic-acid subjects was 7.4% less than in the control subjects, and the incidence of diseases of all sorts was 10.0% less. The diseases were 5% less severe in the ascorbic-acid group than in the placebo group. The differences are not statistically significant, and the investigators themselves concluded that the ascorbic acid had shown no protective effect. Their tables show, however, that the small added intake of ascorbic acid (average 90 mg per day) is associated with an apparent decrease in integrated morbidity of about 12%, and their work should not be quoted as having shown no effect.

CHARLESTON AND CLEGG

Four recent studies were not mentioned by Dykes and Meier. One is the 15-week study carried out with 90 subjects in Glasgow.[17] The 47 ascorbic-acid subjects (1 g per day) had an average of 0.94 colds, with average duration 3.5 days, integrated morbidity 3.29 days of illness per person, and the 43 placebo subjects had an average of 1.86 colds, with average duration 4.2 days, integrated morbidity 7.81 days of illness per person. The observed decrease in integrated morbidity is accordingly 58%. The study was not double-blind, in that one investigator knew the identity of the subjects in the two groups. The observed difference in amount of illness is statistically significant at the level P (one-tailed) <0.002.

ELLIOTT

A 10-week double-blind study of 70 crew members on a Polaris submarine was carried out by Elliott.[18] The 37 subjects in the ascorbic-acid group received 2 g of ascorbic acid per day and the 33 control subjects received a placebo. There was no consistent difference between the two groups in the incidence of ninny nose and sneezing. The average number of days of morbidity for hoarseness, sore throats, nonproductive coughs, and productive coughs was 63%, 72%, 60%, and 69%, respectively, less for the ascorbic-acid subjects than for the placebo subjects, statistically significant by the Wilcoxon sequence one-tailed test for hoarseness (P = 0.0155) and productive coughs (P = 0.0327) but not for the others. I take the average (with 0% for runny nose and sneezing), 44%, as the decrease in integrated morbidity in ascorbic-acid subjects in this study.

SABISTON AND RADOMSKI

Sabiston and Radomski of the Department of National Defense, Canada, have reported the results of a 4-weeks study of 112 soldiers undergoing operational training in northern Canada.[19] Ascorbic acid, 1 g per day, was given to 56 subjects and a placebo to the other 56. Allocation of the 8 men in each tent to one or the other of groups of 4 receiving the two kinds of tablets was made at random. The ascorbic-acid subjects had 6 colds, mean duration 4.3 days, average days of illness per man 0.46, and the placebo subjects had 14 colds, mean duration 5.8 days, average days of illness per man 1.45. The decrease in integrated morbidity is accordingly 68%, statistically significant at the level P (one-tailed) < 0.05.

ANDERSON, BEATON, COREY, AND SPERO

One of the best of the controlled studies is the third Toronto study, reported in April 1975.[20] Of the 448 subjects who completed the 15-week test 150 received a weekly 500-mg vitamin C tablet (two-thirds sodium ascorbate and one-third calcium ascorbate), 152 received a weekly 500-mg time-release capsule of ascorbic acid, and 145 received a placebo tablet with the same appearance and taste as the ascorbate tablet. In addition the subjects were instructed o take an extra tablet or capsule at the onset of any symptom of illness and, if symptoms persisted, to repeat the dose twice at 4-hour intervals on the first day and once every 12 hours for up to 4 more days.

The investigators report for each of the three groups the mean number of days of morbidity per subject with nine signs or symptoms—confined indoors, off work, nose running or plugged, throat soreness, chest soreness or tightness, felt feverish, cold and shivery, limbs aching and heavy, and mentally depressed, no ambition. This mean was less for each of the two vitamin groups than for the placebo group for every one of the nine signs or symptoms, with ratios ranging from 62 to 98%. The averages of the nine values for the two vitamin groups, 75 and 78%, respectively, are nearly the same, and the investigators made other comparisons between the combined vitamin group (302 subjects) and the placebo group. The subjects in each of these two groups were divided into a high and a low subgroup in nine ways, according to age, sex, usual days indoors, contact with young children, frequency in

crowds, daily juice, vitamin supplement, smoking, and episodes involving nasal symptoms. The mean number of days indoors per subject for each of the eighteen vitamin subgroups was less than that for the corresponding placebo subgroup, with the ratio ranging from 48% (for episodes not involving nasal symptoms) to 87%.

The mean number of days indoors per subject was 1.202 for the whole vitamin group and 1.610 for the placebo group, with ratio 75%, -corresponding to 25% less illness for the vitamin group than for the placebo group. The investigators state that "subjects in both vitamin groups experienced less severe illness than subjects in the placebo group, with approximately 25% fewer days spent indoors because of illness ($P < 0.05$)." They point out that the results are similar to those obtained in their first study, in which they found 30% fewer days confined to home ($P < 0.001$), with a larger intake of vitamin C. They also mention that in each study as much protection against non-respiratory illness as against respiratory illness was observed, and suggest again that large doses of ascorbic acid produce "a generalized nonspecific improvement in the host's ability to cope with infection (or possibly any type of stress?)." They express the opinion that "Taken in conjunction with the positive results reported by other investigators, there is now little doubt that the intake of additional vitamin C can lead to a reduced burden of 'winter illness'."

Table 2

Summary of Results of Studies of Decrease in Integrated Morbidity in Ascorbic-acid Subjects Relative to Placebo Subjects

Study	Amount of decrease in illness per person
Dahlberg, Engel, Rydin	10%
Cowan, Diehl, Baker	31
Franz, Sands, Heyl	40
Ritzel	63
Anderson, Reid, Beaton	32
Anderson, Suranyi, Beaton	9
Coulehan et al.	30
Karlowski et al.	20
Charleston, Clegg	58
Elliott	44
Sabiston, Radomski	68
Anderson, Beaton, Corey, Spero	25
Average	36%

DISCUSSION OF THE STUDIES

The amounts of observed decrease in illness per person (integrated morbidity) in ascorbic-acid subjects relative to placebo subjects as reported in 12 controlled trials are given in Table 2. (In the other one of the 13 studies discussed above, that of Wilson et al., the investigators reported a statistically significant decrease in illness for girls and no decrease for boys. Their report does not include information that would permit calculating the values of the integrated morbidity, so that this study is not included in Table 2.) Nine of the thirteen studies have been discussed also by Dykes and Meier, who seem not to have known about the last three in Table 2.

These thirteen studies comprise all of the controlled trials made of ascorbic acid in relation to the common cold with the ascorbic acid or placebo given to subjects over a period of time and with the subjects in good health at the beginning of the trial and exposed to cold viruses in the ordinary way, by casual contact with other people. In. every one of the thirteen trials a positive result was obtained; that is, the ascorbic-acid subjects had less reported illness than the placebo subjects.

The average amount of decrease in illness per person is 36% (Table 2). The three largest values are 58%, 63%, and 68%. It is my opinion that an effect of this magnitude is clinically significant.

These thirteen trials do not support the statement made in the AMA press release of 10 March 1975 that "Vitamin C will not prevent or cure the common cold." There is no evidence for this statement. Instead, all of the evidence, as summarized above, supports the conclusion that vitamin C has some value in controlling the common cold.

The AMA press release also states that "even if vitamin C did prevent or reduce the discomfort of colds, it would be necessary to take two capsules or tablets three times a day for the rest of one's life to make it work." This statement is an exaggeration. The average amount of the vitamin used in the studies shown in Table 2 is 1 g per day. One could presumably obtain 36% protection by taking one 1-g tablet each day. Moreover, in a number of these studies and in work reported elsewhere[21] it has been pointed out that the course of a cold can be modified by the ingestion of several grams of ascorbic acid, beginning as soon as possible after the cold has started. Regnier[22] reported that in a single-blind controlled trial he was able to avert 90% of the colds in his patients by use of a large intake of ascorbic acid. The recommended intake for this purpose is about 1 g per hour for several hours.[22]

ADVERSE REACTIONS

Several investigators[2,9,11] have reported that no adverse reactions were observed in their subjects who received 1 g per day or more of ascorbic acid. Ascorbic acid is a natural substance, present in all living organisms. It is manufactured by almost all animals at a rate corresponding to an intake for man of between 2 g and 20 g per day, and it is accordingly unlikely that Such an intake would be harmful to man. I have given arguments to support the thesis that this intake is in fact the optimum intake, which leads to the best of health.[23]

Dykes and Meier have discussed the question of adverse reactions. Their conclusion is that "there is currently little adequate evidence on either the presence or the absence of serious adverse reactions to such doses of ascorbic acid, although many such reactions have been hypothesized." They suggest that additional studies in this field are needed. I agree that additional studies are needed, but I do not think that it is

justified to refrain from using this valuable substance until the studies have been carried out.

References

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