

[Critical evaluation of vitamin C as a prophylactic and therapeutic agent in colds].

[Article in German]

RITZEL G

Helv Med Acta. 1961 Jan;28:63-8.

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**English translation of this paper was kindly arranged
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<https://www.mv.helsinki.fi/home/hemila>

https://www.mv.helsinki.fi/home/hemila/VitC_colds.htm

<https://www.mv.helsinki.fi/home/hemila/CC.htm> (Cochrane review)

<https://www.mv.helsinki.fi/home/hemila/CC> (Cochrane review references)

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The German text is available at:

https://www.mv.helsinki.fi/home/hemila/CC/Ritzel_1961_ch.pdf

https://www.mv.helsinki.fi/home/hemila/CC/Ritzel_1961_bm.pdf

A short biography of Ritzel:

http://www.mv.helsinki.fi/home/hemila/CC/Ritzel_1989_ch.pdf

A letter to the editor stating that the trial was randomized, placebo-controlled and double-blind was written to JAMA by Ritzel (JAMA 1976;235:1108):

“The placebo was indistinguishable from the 1-gm ascorbic acid tablet. They were given to school children in two skiing courses. The children were randomly separated into two groups. Neither test subjects nor investigators knew whether the children got placebo or vitamin C. A questionnaire was completed daily by the camp physician for each of the 279 participants who were asked about the presence or absence of 11 specific and six nonspecific cold symptoms. Certain of these, such as pharyngitis, bronchitis, and herpes labialis, together with the number of sick days, could be confirmed by the physicians.”

http://www.mv.helsinki.fi/home/hemila/CC/Ritzel_1976.pdf

Ritzel based his work partly on the study by Bessel-Lorck (1959), which is Ritzel’s ref. 15.

The Bessel-Lorck (1959) paper is also available as a translation:

<http://www.mv.helsinki.fi/home/hemila/T2.pdf>

Ritzel’s (1961) paper was the primary reference for Linus Pauling, when he concluded that there was strong evidence that vitamin C would affect the severity and incidence of colds:

Pauling L (1971) The significance of the evidence about ascorbic acid and the common cold. PNAS

<http://www.pnas.org/cgi/reprint/68/11/2678>

<http://www.ncbi.nlm.nih.gov/pmc/articles/PMC389499>

http://profiles.nlm.nih.gov/MM/B/B/G/V/_/mmbbgv.pdf

<http://osulibrary.orst.edu/specialcollections/rnb/31/31-103.html>

Pauling L (1971) Ascorbic acid and the common cold. Am J Clin Nutr

<http://www.ajcn.org/cgi/reprint/24/11/1294>

From the Office of the School Medical Doctor for the City of Basel – Headed by: Dr. G. Ritzel

Critical Evaluation of the Prophylactic and Therapeutic Properties of Vitamin C with Respect to the Common Cold

By G. Ritzel

According to *Szent-Györgyi (1)* a large area of shifting transitions lies between manifest avitaminosis and optimal health. Numerous investigations by diverse authors have attempted to document this hypothesis with respect to conditions of vitamin C deficiency. *Scheunert (2)* confirms on the basis of long term studies involving human beings that vitamins can be sub-optimally supplied, the result of which is that important metabolic reactions are impaired even though hypovitaminotic symptoms may not become manifest.

The therapeutic effect of vitamin C following supplementation with very high daily doses which exceed many times over the doses prescribed for the prevention of scurvy indicates its additional efficacy as a healing substance.

Multiple possible pharmacodynamic effects of the L-ascorbic acid are discussed: virucidal effect (3, 4), improvement in the utilization of energy providers in foodstuffs (5), stimulation of the cortical-adrenal function with change of membrane permeability, and consecutive antiphlogistic, possibly even antitoxic (7,8) effect. It is said that conversion of the ascorbic acid differs as a function of the level of the stimulus, and that as a consequence no valid daily dose requirement can be set. Instead reference can be made only to a variable optimal dose that is suited to the different needs.

Increased use during acute sicknesses, in particular, those illnesses caused by infection may be considered to be safe nowadays (9, 10). Activation of non-specific immune reactions (11) and improvement of the phagocytotic capability of the leucocytes are seen as being possibly responsible for the favorable therapeutic effect (12). Also it is said that large doses of vitamin C make it possible for the organism to handle greater physical demands or that they have a positive influence on the consequences caused by the demands (13).

Ascorbic acid is, however, from the toxicologic standpoint indifferent. The undesirable side effects observed by some authors, such as sleeplessness, fatigue, intestinal and vegetative disorders must, in the light of controlled studies in which much higher doses were used, be viewed as side effects of “impure placebos,” but not as those of the active substance (14).

Previous studies of which we are aware and which concerned the prophylactic efficacy of high doses of vitamin C taken in the absence of other medications and to combat the common cold, the flu, and heavy physical stress lack the comparisons available in double-blind studies. For example, the use of vitamin C as a prophylactic was examined by *Bessel-Lorck (15)* and *Bendel (16)* in part by comparing the results of one year in which treatment was given with the results of the previous year during which no prophylaxis was given. Other authors (17) describe a “significant reduction in the duration of the illness,” but the control group consisted of a collection of untreated persons.

Results of our Studies

We had the opportunity this winter to examine the question of whether vitamin C is an effective prophylactic against infection. We used a self-controlling double-blind design for this therapeutic study that included 279 participants of two 5 to 7 day long ski camps. The subjects in the camps who were compared one with the other provided favorable initial conditions in that they were all of the same age and were receiving the same diet. In one original package for each participant, to each of which was assigned a serial number, either 1.0 g of vitamin C or of a placebo was placed. Each morning such a tablet was distributed to each of the subjects and taken under supervision. There was no opportunity for the subjects to exchange tablets.

The study was double-blinded, neither the study participants nor the camp doctors were aware of the set up of the study.

Each of the subjects was individually asked each day about cold symptoms. Accordingly, the findings were gathered largely on the basis of subjective information, and could only secondarily be partially objectified (by means of temperature measurements, examination of the organs of the throat, auscultation of the lungs, etc.). Camp participants who complained of cold symptoms on the very first day were excluded from the study.

We evaluated the main symptoms of a cold to be pharyngitis, laryngitis, tonsillitis and sore throat; bronchitis and coughing, fever and chills, rhinitis, otitis and ear ache, and herpes labialis. We considered the following to be accompanying symptoms: general muscular pain, headache together with other symptoms, abdominal pain and vomiting together with other symptoms, general feelings of sickness, and “fatigue,” together with other symptoms.

Professionals who had absolutely no connection with personnel involved in the study decoded and statistically evaluated the study results.

Table 1 contains a summary of the main findings; it shows collectively the number of sickness days and the individual symptoms.

The group of people treated with vitamin C showed a reduction in days-sick down to 39%, and reduction of individual symptoms down to 35% of the placebo group. The statistical evaluation in accordance with the four-fold table shows significant differences ($0.001 < P < 0.01$).

Table 1

Prophylaxis for the common cold with vitamin C (1.0 g daily): Occurrence of sickness days and individual symptoms compared with a group treated with placebos

	Treated with Vitamin C	Given placebos	Total
Number of Study Participants	139	140	279
Number of Sickness Days	31	80	111
Number of Individual Symptoms	42	119	161

Table 2

Prophylaxis of the common cold with vitamin C: Occurrence of main and accompanying symptoms compared with a group treated with placebos

	Treated with vitamin C		Given placebo		Total	
	No. of patients	No. of sickness days	No. of patients	No. of sickness days	No. of patients	No. of sickness days
Main symptoms:						
Pharyngitis, laryngitis, tonsillitis, sore throat,	7	10	14	28	21	38
Bronchitis, cough	8	14	13	23	21	37
Fever, chills	8	9	9	12	17	21
Otitis media			1	3	1	3
Rhinitis			2	2	2	2
Herpes labialis			1	3	1	3
Accompanying symptoms:						
Muscle pain, headache, abdominal pain, vomiting, diarrhea, general feeling of sickness	8	9	21	48	29	57

Table 2 contains a breakdown of the aforementioned main and accompanying symptoms.

The group treated with vitamin C shows for the first category a marked reduction of the morbidity of conditions of the organs of the throat and the air passages. The statistical workup permits the conclusion that the difference between the control groups with respect to the occurrence of the first-mentioned findings (conditions of the organs of the throat) is not merely coincidental. Following the same testing method a P of less than 0.01 was also computed here. For the remaining main symptoms no statistically reliable differences could be established. It need not be emphasized that the inability to do this has no negative evidence value; the defect of a limited number of individual findings may be a contributory factor in this regard.

It can also be seen from Table 2 that within the group that was treated with the vitamin, the accompanying symptoms were reported significantly less often; here, too, the difference is statistically significant. Whether there is a causal connection between this finding and a prophylaxis of infection or whether this finding indicates an increase in the capacity to perform physical activities regardless of any infectious event cannot be determined from the acquired data.

The acquired data also provide no information as to whether the ascorbic acid medication was pharmacodynamically effective as a replacement made necessary by an externally induced need or in one of the ways mentioned above. The only question that our investigations can answer affirmatively is whether vitamin C can increase the resistance to infectious noxae. This is expressed by the significant decrease of the morbidity rate with respect to the main symptoms of the common cold.

In this connection, too, evaluation of the results from the therapeutic perspective appeared to us to be of interest. In this regard we compared the average length of sickness for both groups. In the case of the group treated with vitamin C it was 1.8 days versus 2.6 days for the group that received placebos. These averages, too, deviate statistically significantly one from the other ($P < 0.05$; t-distribution).

The dosage of 1 g per day quickly leads to saturation of the organism with vitamin C and beyond that to inundation. The fact that the positive infection prophylaxis reported by other investigators (18, 19) - even though not compared to a control group - was described mainly following daily doses in this same order of magnitude speaks in favor of the effectiveness of vitamin as a remedy.

Discussion

It is difficult to evaluate medicines precisely when in attempting to comprehend their *modus operandi* we are limited to examining symptoms while still in ignorance of their causality. Under the study conditions that prevailed it lay in the nature of the effects of vitamin C in which we were interested that in most cases we could not directly acquire either figurative or measurable, i.e., numerical, data. This was attributable to both external circumstances (ski camps) and internal circumstances (multivalent preparations).

Sources of error in the assessment of the prophylactic and therapeutic effect, which arise during single-blind medicinal testing as well as when several different daily dosages are given to the test subjects (20), were reduced to a minimum by means of the design followed in our investigation. Consequently, because we could not use direct measurement procedures, we had worked out an experimental test plan for testing the effects of medicines that was adapted to the therapeutic problem of interest to us.

A trial using placebos and a double blind design along with a comparison with pharmaceuticals with similar effects is used for assessing subjective criteria. (For example, there is no other reliable and accessible way available for assessing the effect of analgesics on human beings.)

Assessments that are based upon the uncontrolled dispensation of placebos that are reported in publications such as “Therapeutic Experiences with . . . “ disregard existing difficulties. Such publications are partly responsible for the fact that the therapeutic sector of medicine - because it is less credible - is less successful than the diagnostic sector.

Particularly plentiful are the hapless wanderings with respect to assessing the therapeutic effects of multivalent preparations. In this regard much is written, but little is said. Expressions such as “I like to give” are just as popular as they are meaningless. One also hears “propitious harmony of the effective components” when the speaker doesn’t even know what synergism means in the context of pharmacology. If a medicine has never reliably proved itself anywhere, it is nevertheless often recommended as a “prophylaxis” to be used “in convalescence” or “in geriatrics.” Such an attitude, which is creative of uncritical confusion, can lead (in an advertisement) to “the cardiac neurosis” being proclaimed to be the “main province of a salve”! This approach is in my opinion outdone by proponents of *Niehan's* therapy (21), who recommend injections of Broca's convolution as a therapy for speech disorders caused by birth trauma.

Therapeutic research would, however, be ill served if one limited one’s interest exclusively to pharmaceuticals whose effects can be comprehended only through laboratory diagnosis or in an otherwise easily objectified manner. Such a unilateral approach fails with regard to numerous therapeutic questions without having thereby demarcated available knowledge. As shown by the subject investigation, methods (22 – 26) have been taught with the help of which sensations can be reliably studied. According to *Green* (27) wherever the value of a treatment is in doubt – whether old or new- there exists a higher moral duty to critically examine, rather than to continue to prescribe the same old thing year after year, just because that is the way that it has always been done.

It is in the spheres of university medicine where the burden is being carried with respect to such pressing questions of therapeutic research, and where attempts are being made to objectify subjective criteria.

Summary

The possibility of preventing infection by the administration of vitamin C was investigated in a moderately large test population during a period of increased exposure. The trial was conducted in such a way as to exclude sources of error in assessing subjective symptoms. Statistical evaluation of the results confirmed the efficacy of vitamin C in the prophylaxis and treatment of colds. Problems of therapeutic research with respect to multivalent preparations which have to be judged chiefly on the basis of subjective symptoms are discussed.

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