Vitamin E supplementation and respiratory infections in older people

Hemilä, Harri

2007

Hemilä, H 2007, 'Vitamin E supplementation and respiratory infections in older people'

http://hdl.handle.net/10138/225894
https://doi.org/10.1111/j.1532-5415.2007.01263.x

Downloaded from Helda, University of Helsinki institutional repository.

This is an electronic reprint of the original article.

This reprint may differ from the original in pagination and typographic detail.

Please cite the original version.
activity may be consistent with heightened baroreceptor
in the midfrequency region representative of baroreceptor
onstrated that peak increase in transfer function magnitude
evaluated using frequency domain analysis. One study dem-
ceptor sensitivity after carotid endarterectomy has been
sustained increase in baroreceptor sensitivity.4 Baroreceptor
after carotid endarterectomy that may be a consequence of
sensitivity in the postoperative period and at 5-year follow-up. Significantly
in patients with increased baroreceptor sensitivity in the
Significantly lower systolic blood pressures were observed
after three maneuvers: Valsalva, angiotensin-induced vaso-
striction, and nitroglycerin-induced vasodilatation.

mechanism of hypotension after carotid endarterectomy
may involve greater baroreceptor sensitivity. Baroreceptors
are sensory receptors sensitive to stretch from increased
pressure that function as part of a central reflex to reduce
that pressure.1 Baroreceptor reflex responses to carotid
endarterectomy may involve removal of stiff atheromatous
plaque, which improves arterial blood flow, allowing
increased lateral pressure to be placed on the carotid
artery lumen, which increases carotid sinus distension. The
resultant stretching of the carotid sinus wall activates
baroreceptors and a reflex response of heightened para-
sympathetic tone, thus inducing arterial vasodilatation,
hypotension, and bradycardia.

Several observational studies have noted hypotension
after carotid endarterectomy in the immediate postopera-
tive setting that persisted weeks after surgery.2–5 Barore-
ceptor sensitivity after carotid endarterectomy has been
evaluated using frequency domain analysis. One study dem-
strated that peak increase in transfer function magnitude
in the midfrequency region representative of baroreceptor
activity may be consistent with heightened baroreceptor
sensitivity after carotid endarterectomy.5 Author study
showed decreases in blood pressure readings up to 5 years
after carotid endarterectomy that may be a consequence of
sustained increase in baroreceptor sensitivity.4 Baroreceptor
sensitivity was estimated as the change in pulse interval in
ms/mmHg change in blood pressure taken as an average
after three maneuvers: Valsalva, angiotensin-induced vaso-
constriction, and nitroglycerin-induced vasodilatation.
Significantly lower systolic blood pressures were observed
in patients with increased baroreceptor sensitivity in the
postoperative period and at 5-year follow-up. Significantly
diminished systolic and diastolic blood pressure ranges were
also observed in patients with increased baroreceptor
sensitivity in the postoperative period and at 5-year follow-up.

It is possible that our patient’s initial hypotension after
carotid endarterectomy and the subsequent moderation of
hypertension severity, as suggested by fewer antihyperten-
sive medicines being required, may be the consequence of
greater baroreceptor sensitivity. If the increase in barore-
ceptor sensitivity is sustained, carotid endarterectomy may
offer a potential secondary benefit of long-term improve-
ment in hypertension and blood pressure variability in ad-
tion to the primary goal of lowering stroke risk. Furthermore, in the acute period after carotid endarterec-
tomy, geriatricians should be aware of the potential for
baroreceptor-mediated hypotension as vigilant blood
pressure monitoring and titration of antihypertensive
medication may become essential.

Emre Noteroglu, MD
George A. Kuchel, MD
UConn Center on Aging
University of Connecticut Health Center
Farmington, Connecticut

Figure 1. Systolic and diastolic blood pressure readings at base-
line and during 3 weeks of postoperative follow-up. HCTZ = hydrochlorothiazide.

ACKNOWLEDGMENTS

Financial Disclosure: The authors did not receive any grant
support or honoraria from related industry. The authors do
not have stock or patents in medically related companies.
Neither author participates in speaker’s forums concerning
the subject matter of this letter.

Author Contributions: Dr. Emre Noteroglu: coauthor.
Dr. George Kuchel: coauthor and mentor.

Sponsor’s Role: There are no sponsors.

REFERENCES

1. Thrasher TN. Baroreceptors, baroreceptor unloading, and the long-term control of
2. Bove EL, Fry WJ, Gross WS et al. Hypotension and hypertension as conse-
quences of baroreceptor dysfunction following carotid endarterectomy. Surgery
3. Dodds SR, Finch D, Chant AD. Early effect of carotid endarterectomy on ar-
terial blood pressure measured with an ambulatory monitor. Br J Surg
1997;84:1104–1106.
4. Hirschl M, Kundi M, Blazek G. Five-year follow-up of patients after
thromboendarterectomy of the internal carotid artery: Relevance of barorecep-
5. Landesberg G, Adam D, Berlatzky Y et al. Step baroreflex response in awake
patients undergoing carotid surgery: Time- and frequency-domain analysis. Am

VITAMIN E SUPPLEMENTATION AND
RESPIRATORY INFECTIONS IN OLDER PEOPLE

To the Editor: I read with great interest the Liu et al.1 study
examining the effect of multivitamin and mineral supple-
mentation on infections in nursing home residents, al-
though no rationalization for the supplement composition
was described. In the large-scale Alpha-Tocopherol, Beta-
Carotene (ATBC) Study with male smokers aged 50 to 69 at
baseline, 20 mg/d β-carotene increased mortality2 and had
no effect on common cold incidence in 2,005 participants
aged 65 and older3 or on pneumonia incidence in 2,985
participants aged 65 and older.4 Therefore, the inclusion of
16 mg/d of β-carotene in the supplement1 would call for an
explicit motivation, and the previous negative results
should have been cited. In our further analysis of common
cold incidence in the ATBC Study cohort, we found inter-
action between vitamin E and β-carotene supplementation
(unpublished data), and therefore we restricted the more-
detailed vitamin E analysis to participants who were not
administered β-carotene.5
Several trials examining the effect of vitamin E on respiratory infections in older people have been published (Table 1), yet Liu mentioned only the trial by Meydani et al.6 Another controlled trial7 with elderly Dutch people found no effect of vitamin E on the incidence of respiratory infections (Table 1), although vitamin E supplementation increased the number of symptoms (P = .03), the duration of illness (P = .02), the percentage of participants with fever (P = .009), and restriction of activity (P = .02). Thus, vitamin E may be harmful for some elderly people.

Other recent findings also suggest that vitamin E supplementation may be harmful. In the ATBC Study cohort, the effect of vitamin E on the incidence of the common cold diverged in older people.5 In participants aged 72 and older, vitamin E increased the risk of getting the common cold 58% in those who smoked heavily and did not live in cities, whereas it reduced common cold risk 46% in city dwellers who smoked less. The confidence intervals of these two subgroups are spectacularly far from each other (Table 1). Thus, there is strong evidence that older people are heterogeneous with regard to the effects of vitamin E on incidence of the common cold.

In the ATBC Study cohort, the age of smoking initiation significantly modified the effect of vitamin E on pneumonia incidence, indicating heterogeneity in the effects of the vitamin.4 In a subgroup analysis, we also found that vitamin E reduced the risk of pneumonia in participants who exercised in their leisure time (Table 1). Such heterogeneity limits the possibility of generalizing findings of trials.

Furthermore, in Liu’s Table 4,1 the analysis of antibiotic treatment is inappropriate. Although we may assume that “antibiotic courses” are independent observations, “antibiotic days” definitely are not independent, because a course of antibiotics consists of approximately 10 days directly linked to each other. The authors should have used, for example, the t-test to analyze whether the mean duration of antibiotic courses differed between the study groups. Thus, the small P-value in Liu’s Table 4 is not valid.

Finally, Liu refers to Chandra’s 1992 report11 without noting that a later publication, based on the same 1992 cohort, was retracted because of data fabrication,12,13 and serious doubts about the original 1992 article were also expressed because of various statistical inconsistencies.13,14 Although vitamin E may affect the immune system in older people, the findings for clinical infections are mostly negative, and there is evidence of harm for some people. Therefore, vitamin E self-supplementation should be discouraged until those who might benefit from supplementation are identified accurately.

Harri Hemilä, MD, PhD
Department of Public Health
University of Helsinki
Helsinki, Finland

ACKNOWLEDGMENTS

Financial Disclosure: No financial support or conflicts.

Author Contributions: Harri Hemilä is the sole contributor to the paper.

Sponsor’s Role: None.

REFERENCES


Table 1. The Effect of Vitamin E Supplementation on the Incidence of Respiratory Infections in Older People

<table>
<thead>
<tr>
<th>Study (ref.)</th>
<th>Vitamin E Dose (mg/d)</th>
<th>Age</th>
<th>Person-Years</th>
<th>Outcome</th>
<th>Risk Ratio (95% Confidence Interval)</th>
<th>Subgroup; Notes</th>
</tr>
</thead>
<tbody>
<tr>
<td>Hemilä et al. 2002</td>
<td>50</td>
<td>≥65</td>
<td>8,020</td>
<td>Common cold</td>
<td>0.95 (0.90–1.00)</td>
<td></td>
</tr>
<tr>
<td>Meydani et al. 2004</td>
<td>200</td>
<td>≥65</td>
<td>539</td>
<td>URI</td>
<td>0.88 (0.73–1.05)</td>
<td>Table 3 (ITT)</td>
</tr>
<tr>
<td>Liu et al. 2007</td>
<td>44</td>
<td>≥65</td>
<td>929</td>
<td>URI</td>
<td>0.92 (0.75–1.12)</td>
<td></td>
</tr>
<tr>
<td>Graat et al. 2002</td>
<td>200</td>
<td>≥60</td>
<td>787</td>
<td>URI + LRI</td>
<td>1.12 (0.88–1.25)</td>
<td></td>
</tr>
<tr>
<td>Harim &amp; Miller 1986</td>
<td>200–400</td>
<td>≥70 (77%)</td>
<td>51</td>
<td>LRI</td>
<td>1.07 (0.68–1.68)</td>
<td>Aged 24–104; 23% aged &lt; 70</td>
</tr>
<tr>
<td>Hemilä et al. 2004</td>
<td>50</td>
<td>≥65</td>
<td>16,117</td>
<td>Pneumonia</td>
<td>0.94 (0.70–1.24)</td>
<td></td>
</tr>
<tr>
<td>Hemilä et al. 2008</td>
<td>50</td>
<td>≥60</td>
<td>3,704</td>
<td>Pneumonia</td>
<td>0.08 (0.01–0.61)</td>
<td>Exercising during leisure</td>
</tr>
<tr>
<td>Meydani et al. 2004</td>
<td>200</td>
<td>≥65</td>
<td>539</td>
<td>LRI</td>
<td>1.00 (0.80–1.26)</td>
<td>Table 3 (ITT)</td>
</tr>
<tr>
<td>Liu et al. 2007</td>
<td>44</td>
<td>≥65</td>
<td>929</td>
<td>LRI</td>
<td>0.91 (0.75–1.10)</td>
<td></td>
</tr>
</tbody>
</table>

*Participants not administered β-carotene.

ITT = intention-to-treat analysis; LRI = lower respiratory infection; URI = upper respiratory infection.
RESPONSE LETTER TO DR. HEMILÄ

To the Editor: Dr. Hemilä raises the issue of the composition of the supplement used in our study, in particular the beta-carotene content, and he cites additional studies evaluating the effects of vitamin E. The composition of the multivitamin/mineral supplementation used in our study was chosen to meet or slightly exceed the Dietary Reference Intake for most nutrients. The literature available at the time of the planning of the study, including a study in which the validity has been seriously questioned, guided the composition of the supplement.1 Nevertheless, other studies examining effects on infectious episodes have used formulations similar in composition to our intervention supplement.2–4 We also took into consideration the composition of commonly available over-the-counter vitamin and mineral supplemenations.

We were aware of the association between beta-carotene and lung cancer in male smokers. We were also aware of a negative association between beta-carotene and lung cancer found in a study of 22,000 physicians.5 Several of the studies cited in Dr. Hemilä’s letter are based on the same group of community-dwelling male smokers aged 50 to 69 from the Alpha-Tocopherol, Beta-Carotene Study.6 Although this is an important study, we question the generalizability and relevance of those results to our study population of older, mostly female, nonsmoking nursing home residents. The study by Graat et al.7 included older community-dwelling subjects, whereas our study focused on an institutionalized population, as did the Meydani publication.8 It was not our intention to provide a comprehensive review of papers published on vitamin E. Our study focused on the use of combination multivitamin and mineral supplementation, not specific micronutrients. The association between antioxidant supplementation and greater mortality has been documented in studies using doses higher than that provided in our study.9 Given the high rate of suboptimal intake of several nutrients (Table 5),10 including vitamin E (unpublished), the supplementation provided in our study would have served to bring subjects up to or just slightly above the daily required nutrient intake, not into the range of high-dose supplementation. We thank the letter writer for pointing out two typographical errors in Table 4. We used Wilcoxon rank sum tests (t tests are not appropriate, because the outcomes were not normally distributed) to assess differences between the multivitamin supplementation and control groups for these secondary outcomes. For antibiotic days, the P-value in the second row should read .02.

Finally, we are aware of the concerns raised in the scientific community regarding authenticity of Dr. Chandra’s work and indicated that his paper was considered “controversial” in our discussion. Despite the negative results reported in two recent meta-analyses,11–13 the authors of those meta-analyses conclude that further studies are required, particularly in high-risk populations, such as nursing home residents. We believe that our study makes a worthy contribution in this area.

Barbara A. Liu, MD
Department of Medicine
Sunnybrook Health Sciences Centre
Regional Geriatric Program of Toronto
Department of Medicine
University of Toronto
Toronto, Canada

Allison McGeer, MD
Department of Microbiology
Mount Sinai Hospital
Department of Medicine
University of Toronto
Toronto, Canada

Margaret A. McArthur, RN
Department of Microbiology
Mount Sinai Hospital
Toronto, Canada

Andrew E. Simor, MD
Department of Medicine
Department of Microbiology
Sunnybrook Health Sciences Centre
Department of Medicine
University of Toronto
Toronto, Canada

Elahab Aghdassi, PhD
Department of Medicine
Toronto General Hospital
Toronto, Canada

Lori Davis, PhD
Department of Public Health Sciences
University of Toronto
Toronto, Canada

Johane P. Allard, MD
Department of Medicine
Toronto General Hospital
Department of Medicine
University of Toronto
Toronto, Canada