Dietary vitamin C intake is inversely related to cough and wheeze in young smokers

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Abstract  We aimed to investigate whether dietary vitamin C intake, an important antioxidant, is inversely related to self-reported respiratory symptoms in young adults of a community. A random sample of 4300 subjects, aged 20 – 44 years, living in Bergen, Norway, received a postal questionnaire on respiratory symptoms; 80% responded. Vitamin C intake (mg per week) was estimated from a food-frequency questionnaire asking how often the subject had consumed units of orange juice, oranges, potatoes, carrots and tomatoes. Significant differences in the intake of vitamin C were observed across smoking categories with current smokers having the lowest intake, while there was no variation by gender, age or occupational dust exposure. Dietary vitamin C intake was inversely related to "morning cough", "chronic cough", "wheeze" and "wheeze ever". After adjusting for gender, age, body mass index, "occupational exposure" pack-years as well as having and stratified on smoking habits in multiple logistic regression analyses, the relationship between dietary vitamin C intake and "cough" and "wheeze" tended to be associated to smoking. The odds ratio (OR) for "morning cough" was 0.68 (95% CI: 0.35–0.95), "chronic cough" OR 0.69 (95% CI: 0.47–1.04) and "wheeze ever" OR 0.75 (95% CI: 0.56–1.01) in current-smokers with dietary vitamin C intake in the upper (>395 mg/week) vs. the lower (<209 mg/week) tertile. The OR for "wheeze" was 0.56 (95% CI: 0.35–0.88) in ex-smokers. The magnitude of these effects remained after excluding subjects with supplementary vitamin C intake (n=199) from the statistical analyses. Among young Norwegian adults, having a low prevalence of asthma and high prevalences of smoking-related respiratory symptoms, dietary vitamin C intake may act as an antioxidant and thereby reduce cough and wheeze in smokers having high oxidant stress.

INTRODUCTION

In the natural, oxygen-rich environment of the lungs, the toxic effects of oxidants are carefully balanced by several antioxidant defense systems supporting normal cellular function (1). An increase in exogenous or endogenous oxidative stress or a decrease in antioxidant capacity can lead to tissue damage and dysfunction.

Cigarette smoking increases the oxidant stress and therefore the antioxidant burden on the lungs and stimulates neutrophils and macrophages to enhance the production of proteases and oxidants, which in turn can inactivate protease inhibitors (2). These changes could lead to a protease—antiprotease imbalance within the alveolar structures and to the development of chronic inflammation (3) and emphysema (4). The established role of oxidants in lung tissue injury and disease has promoted the hypothesis that antioxidants may act as preventive agents. Many studies have shown that high intake of vitamin C or fruits, rich in vitamin C, are associated with higher lung function (5,6) with very similar effect estimates (7–12). However, if there is a beneficial association of vitamin C intake with respiratory symptoms is still less consistent. Some studies have shown effects on respiratory symptoms of dietary vitamin C intake (13,14), while others have not (15,8,16). Furthermore, it is still unclear if these effects may be limited to some specific groups, for example by age and smoking status (17).

The aim of the present study was to investigate the relationship between dietary consumption of vitamin C, one of the main antioxidants in the diet, and respiratory symptoms among young adults of a Norwegian community.
METHODS

Population sample

This cross-sectional study, in the city of Bergen, Norway, was performed as part of the European Community Respiratory Health Survey (18). A random sample of 4300 subjects from the general population of Bergen, Norway, aged 20–44 years, were sent a postal questionnaire on October 1, 1991 plus two additional reminder letters if there was no response; 3450 subjects (80%) responded. Of those responding 51% were females, and the response rate increased with age (19). The study was approved by the Regional Committee of Medical Research Ethics, University of Bergen.

Questionnaire

Dietary habits were assessed by a semiquantitative food-frequency questionnaire by asking: “How often, on average the last year, did you consume the following nutrients?”. Nine options were given (never or less than 1 a day, 2–4 per week, 5–6 per week, 1 per day, 2–3 per day, 4–5 per day, >6 per day). The units for the dietary items were: orange juice 150 ml, one orange 150 g, one potato 80 g, one-half carrot raw or boiled 37 g, one tomato 65 g, fish 150 g, coffee 150 ml, tea 150 ml and Pepsi or Coca-Cola 300 ml. In addition, subjects were asked if they took a supplement of vitamin C the last year and the same nine options of answering was given. The questionnaire was originally developed by Channing Laboratory, Harvard Medical School, and has documented acceptable reproducibility and validity (20).

The amount of vitamin C in the following dietary items per unit are: orange juice 50 mg, orange 80 mg, potato 7 mg, carrot 2 mg, tomato 11 mg (21). None of the other dietary items enquired about contained vitamin C. A variable was created from the five dietary items containing vitamin C indicating the relative amount of vitamin C in the diet: (orange juice*50 + orange*80 + potato*7 + carrot*2 + tomato*11). The original nine options of answering the dietary questions was then reclassified in units per week creating a continuous vitamin C variable (mg/week).

Information about four respiratory symptoms was obtained by asking: “Have you had wheezing or whistling in your chest at any time in the last 12 months?” (wheeze); “Have you woken up with a feeling of tightness in your chest at any time in the last 12 months?” (chest tightness); “Have you been woken by an attack of shortness of breath at any time in the last 12 months?” (breathless at night); “Have you had an attack of asthma in the last 12 months?” (asthma attack) (18). In addition, three BMRC-modified questions were asked (22): “Do you usually cough or clear your throat in the morning?” (morning cough); “Do you have cough for 3 months or more altogether during a year?” (chronic cough); “Do you ever have wheezing in your chest?” (wheeze ever).

Never-smokers were individuals who had never smoked daily; ex-smokers were those who had smoked daily and quit; smokers were those who were smoking daily at the time of the study. Ever-smokers were ex-smokers and smokers together. Lifetime smoking was assessed as pack-years estimated as the duration of smoking in years multiplied by the average number of cigarettes smoked per day and divided by 20 (19).

Occupational exposure was assessed by asking: ‘In your occupation, have you worked with or been exposed to mineral- or metal-dust in the last 12 months?” (asbestos, stone dust, rock dust, sandblasting, rockwool, glass wool, paint pigments with chromium, cement dust, textile or tannic dye colors with chromium, dust from nickel in electronic products, dust from cadmium alloys). The answers were coded into four exposure categories (never, every month or less, every week, every day) (“occupational exposure”). The body mass index (kg/m²) was calculated from self-reported weight (kg) and height (m).

Statistical methods

Due to the skewed nature of our measure of vitamin C intake (Fig. 1), summary statistics for this are expressed in terms of median and interquartile range rather than as means and standard deviations. For the data in Tables 1–3, we divided vitamin C intake into tertiles. We used chi-square test and analysis of variance to compare vitamin C intake in different subgroups (Table 1). In Tables 2 and 3, we used logistic regression to relate vitamin C intake to respiratory symptoms (dichotomous response variables). In Table 2, the significance probability for relationship between dietary vitamin C intake and seven respiratory symptoms are given both before and after adjustment for smoking habits.

The number of subjects included in each analysis varies somewhat due to missing values. Information on occupational mineral- or metal-dust exposure was missing for about 17% of the subjects. In Table 4 subjects with missing values on “occupational exposure” were categorized as non-exposed.

Unless otherwise noted, all P-values are two-sided and the term “significant” implies a P-value < 0.05. All analyses were conducted using the BMDP statistical software package (23).

RESULTS

Characteristics of the population

Table 1 shows the percent of females, mean age, mean body mass index, pack-years smoked and present
occupational dust or gas exposure by dietary vitamin C intake and smoking status. We observed a significant variation of gender and age across the tertiles of dietary vitamin C intake, while no variation was observed for body mass index, pack-years of smoking nor for occupational dust or gas exposure.

**Vitamin C intake**

The median dietary vitamin C intake was 286 mg/week (range: 18, 25–6263 mg, interquartile range: 144–430 mg). Vitamin C consumption varied significantly between never-smokers (median: 304 mg/week; interquartile range: 149–459 mg), ex-smokers (median: 321 mg/week; interquartile range: 172–470 mg) and smokers (median: 256 mg/week; interquartile range: 130–382 mg). Altogether 312 subjects were daily taking a supplement of vitamin C.

**Respiratory symptoms**

The prevalences of respiratory symptoms were: “morning cough” 24%, “chronic cough” 9%, “wheeze” 25%,
“wheeze ever” 44%, “chest tightness” 12%, “breathless at night” 5% and “asthma attack” 3%. The prevalences of respiratory symptoms by levels of vitamin C intake and smoking habits are shown in Table 2. The rates of “morning cough”, “chronic cough”, “wheeze” and “wheeze ever” showed in logistic regression a significant decreasing trend with increasing vitamin C consumption (Table 2) also after adjusting for smoking habits. The inverse relationship between vitamin C intake and “morning cough”, “wheeze” and “wheeze ever” appeared to vary by smoking-status since the interaction terms between dietary vitamin C intake and smoking were significant or borderline significant (Table 2). No relationship between vitamin C intake and “chest tightness”, “breathless at night” or “asthma attack” was observed.

**Multiple logistic regression analyses**

Adjusted OR for respiratory symptoms by different predictor variables, in logistic regression models, are shown
Table 3. Adjusted OR with 95% confidence intervals (CI) for respiratory symptoms with respect to dietary vitamin C intake and possible confounding predictor variables in multivariate logistic regression models.

<table>
<thead>
<tr>
<th>Predictor variables</th>
<th>Morning cough</th>
<th>Chronic cough</th>
<th>Wheeze&lt;sup&gt;a&lt;/sup&gt;</th>
<th>Wheeze ever</th>
<th>Breathless at night&lt;sup&gt;a&lt;/sup&gt;</th>
<th>Chest tightness&lt;sup&gt;a&lt;/sup&gt;</th>
<th>Asthma attack&lt;sup&gt;a&lt;/sup&gt;</th>
</tr>
</thead>
<tbody>
<tr>
<td></td>
<td>OR</td>
<td>95% CI</td>
<td>OR</td>
<td>95% CI</td>
<td>OR</td>
<td>95% CI</td>
<td>OR</td>
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<tr>
<td><strong>Vitamin C intake</strong>&lt;sup&gt;a&lt;/sup&gt; (n=2405)</td>
<td></td>
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<tr>
<td>Lower tertile (&lt;209 mg/week)</td>
<td>1.00</td>
<td>1.00</td>
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<td>1.00</td>
<td>1.00</td>
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<tr>
<td>Middle tertile</td>
<td>0.69</td>
<td>0.54–0.88</td>
<td>0.87</td>
<td>0.61–1.25</td>
<td>1.15</td>
<td>0.91–1.49</td>
<td>1.04</td>
</tr>
<tr>
<td>Upper tertile (≥395 mg/week)</td>
<td>0.70</td>
<td>0.55–0.90</td>
<td>0.76</td>
<td>0.52–1.01</td>
<td>0.86</td>
<td>0.67–1.12</td>
<td>0.84</td>
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<tr>
<td><strong>Confounders</strong></td>
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<tr>
<td>Age (increase of 10 years)</td>
<td>1.11</td>
<td>0.96–1.28</td>
<td>1.11</td>
<td>0.89–1.38</td>
<td>1.27</td>
<td>1.09–1.47</td>
<td>1.22</td>
</tr>
<tr>
<td>Sex (♂=male, ♀=female)</td>
<td>1.08</td>
<td>0.85–1.36</td>
<td>1.01</td>
<td>0.72–1.42</td>
<td>1.12</td>
<td>0.89–1.38</td>
<td>1.33</td>
</tr>
<tr>
<td>Body mass index (increase of 5 kg/m&lt;sup&gt;2&lt;/sup&gt;)</td>
<td>1.02</td>
<td>0.98–1.05</td>
<td>1.09</td>
<td>1.03–1.14</td>
<td>1.06</td>
<td>1.02–1.09</td>
<td>1.02</td>
</tr>
<tr>
<td>Occupational dust exposure&lt;sup&gt;a&lt;/sup&gt; (0=no, 1=yes)</td>
<td>1.35</td>
<td>1.04–1.75</td>
<td>1.05</td>
<td>0.71–1.56</td>
<td>1.53</td>
<td>1.18–2.00</td>
<td>1.37</td>
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<tr>
<td>Never-smoker</td>
<td>1.00</td>
<td>1.00</td>
<td>1.00</td>
<td>1.00</td>
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<td>1.00</td>
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<tr>
<td>Ex-smoker</td>
<td>1.04</td>
<td>0.72–1.47</td>
<td>0.92</td>
<td>0.49–1.72</td>
<td>1.30</td>
<td>0.92–1.82</td>
<td>1.71</td>
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<tr>
<td>Smoker (1–9 cigarettes/day)</td>
<td>1.62</td>
<td>1.04–2.52</td>
<td>1.69</td>
<td>0.82–3.52</td>
<td>2.19</td>
<td>1.45–3.31</td>
<td>2.17</td>
</tr>
<tr>
<td>Smoker (≥10 cigarettes/day)</td>
<td>5.46</td>
<td>4.34–7.14</td>
<td>4.76</td>
<td>3.22–7.14</td>
<td>5.55</td>
<td>4.34–7.14</td>
<td>3.85</td>
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</table>

<sup>a</sup>Reported during the last 12 months.
<table>
<thead>
<tr>
<th>Predictor variables</th>
<th>Morning cough</th>
<th>Chronic cough</th>
<th>Wheeze**</th>
<th>Wheeze ever</th>
<th>Breathless at night**</th>
<th>Chest tightness**</th>
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<tr>
<td></td>
<td>OR 95% CI</td>
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<td><strong>Vitamin C intake in never-smokers</strong> (n=993)</td>
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<td>1.00</td>
<td>1.00</td>
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<td>1.00</td>
<td>1.00</td>
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<tr>
<td>Middle tertile</td>
<td>0.82</td>
<td>0.49–1.35</td>
<td>1.28</td>
<td>0.57–2.94</td>
<td>1.14</td>
<td>0.81–1.61</td>
<td>1.07</td>
</tr>
<tr>
<td>Upper tertile (≥395 mg/week)</td>
<td>0.91</td>
<td>0.56–1.47</td>
<td>0.72</td>
<td>0.30–1.75</td>
<td>0.95</td>
<td>0.68–1.33</td>
<td>1.09</td>
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<td><strong>Vitamin C intake in ex-smokers</strong> (n=531)</td>
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<td><strong>Vitamin C intake in smokers</strong> (n=1299)</td>
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<td>0.87</td>
<td>0.65–1.14</td>
<td>0.75</td>
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*Adjusted for age, gender, body mass index, pack-years and occupational dust exposure. Subjects with missing data on occupational dust exposure were categorized as non-exposed.

**Reported during the last 12 months.
in Table 3. After adjusting for age, sex, body mass index, “occupational exposure” and smoking habits, vitamin C intake was significantly inversely related to “morning cough”, but it also appeared to be related to “chronic cough”, “wheeze” and “wheeze ever”. Excluding subjects (n=312) taking daily vitamin C supplementation resulted in effects of similar magnitude as those presented in Table 2.

Analyses stratified on smoking habits adjusting for gender, age, body mass index, pack-years and “occupational exposure”, showed that the relationship between dietary vitamin C intake and symptoms of “cough” and “wheeze” were mainly associated with smoking (Table 4). The magnitude of the OR shown in Table 4 remained after excluding subjects taking daily supplemental vitamin C (199 ever-smokers and 113 never-smokers) or those with missing data on “occupational exposure”.

DISCUSSION

We observed, in this cross-sectional community study, that dietary intake of vitamin C mainly appeared to be inversely related to symptoms of “cough” and “wheeze” in young current-smokers. We did not observe this relationship for “chest tightness”, “breathless at night” and “asthma attack”.

The random sample examined should be representative of the study population (19). Both the questionnaire on respiratory symptoms (22,24) and the semi-quantitative food-frequency questionnaire (20) have been validated. A recent study comparing a self-administered food-frequency questionnaire, as well as an interview-administered questionnaire with a 7-day food recording, reported good validity when using the former method to estimate nutrient intake (25).

A high intake of vitamin C in the diet was associated with never- and ex-smoking in our study. Vitamin C intake as a predictor variable of the seven respiratory symptoms analyzed must therefore be interpreted with caution, since vitamin C intake may be a proxy for other dietary factors not included in the present analyses or registered in the questionnaire (vitamin E and total energy intake in the present study). On the other hand, the vitamin C variable in this study was composed of several main dietary items and should therefore be robust to unwanted bias.

The confounding variables of age, sex, body mass index, smoking habits and “occupational gas and dust exposure” have been taken into account to estimate the true effect of vitamin C intake on asthma-like symptoms. Smoking habits are a main risk factor for respiratory symptoms, which was also observed in the present study. Furthermore, “occupational exposure” was a significant predictor variable of “wheeze”, “wheeze ever”, “chest tightness” and “morning cough”. “Occupational exposure” may also be looked upon as a variable taking into account other socio-economic differences in this community than smoking can do on its own. This may be an argument in favor of including this confounding variable in the analyses. Owing to a relatively high proportion of missing data for “occupational exposure”, the inclusion of this variable would have reduced the statistical power of the multivariate analyses unfavorably. Whether we excluded subjects with missing values or categorized them as non-exposed, the magnitude of the ORs remained basically stable.

Epidemiological studies have consistently demonstrated lower levels of pulmonary function in individuals who consume lower levels of vitamin C or food containing vitamin C (5–12). However, if there is a beneficial association between dietary vitamin C intake and respiratory symptoms, then development of asthma or pulmonary diseases are still less consistent. High dietary intake and raised serum concentrations of vitamin C had a protective effect against respiratory symptoms in children from Italy (14), in a representative sample of adults in the United States (13) and in adults from Scotland (26). However, other studies have not showed such an association (15,16,27,8). Furthermore, data from prospective studies of the development of asthma and pulmonary disease show different effects of the consumption of fruit and vitamin C. The Zutphen study suggested that fruit, but not specifically vitamin C, was inversely related to the development of chronic non-specific lung disease (28). However, The Nurses’ Health Study demonstrated no relationship between dietary vitamin C intake and the subsequent incidence of asthma in a large cohort of 77,866 women (15). Differences in gender of the subjects, the outcome measures, smoking habits might explain the observed differences. Alternatively, a protective effect of fruit may be attributable to fruit constituents other than vitamin C.

British and Dutch male heavy smokers not only have a lower dietary antioxidant intake than never-smokers (29), but additionally seem to use supplementation relatively infrequently (30). This may in turn exacerbate the damage caused by smoking. In a Finnish study of almost 30,000 subjects, no effect of supplementation with alpha-tocopherol or beta-carotene was observed on the symptoms of chronic obstructive pulmonary disease (31). However, beneficial effect of dietary intake of fruits and vegetables rich in these compounds was observed (31). Thus, there might be differences in health effects if the intake of vitamins comes from food or if taken as a supplement. In our study, 15% used a supplement of vitamin C daily during the last year. When excluding these subjects from the analyses, the effects of dietary vitamin C intake on the respiratory symptoms remained.

In this study, the effects of dietary intake of vitamin C was observed in smokers only and supports a previous published study (10). The level of oxidant stress is higher
in smokers than in non-smokers and the effect of antioxidant agents may find a much better playground in smokers (32). However, we cannot exclude the health effects in non-smokers, but these effects must be small and might only be observed in much larger population studies than the present.

Our study is limited to young adults aged 20—44 years of age. Even in this young age group, smoking was strongly associated with respiratory symptoms of cough and wheeze. It is an interesting question for future research whether the effects of dietary vitamin C intake may vary by age as the respiratory symptoms and processes by time may have inferred more persistent damages of the airways.

In the present study, a median intake of approximately 40 mg vitamin C was observed, which is lower than the 60 mg/day that is recommended. The differences in vitamin C intake between current smokers on the one hand and never- and ex-smokers on the other, equivalents to about 7—9 potatoes/week. One may speculate that such small differences in vitamin C consumption might have a limited clinical effect on symptoms and disease. However, when a dietary effect on respiratory symptoms can be indicated in our population with a generally low vitamin C intake, greater effects might be found in other populations with a higher intake.

A great and so far unexplained variation in respiratory symptoms has been observed between and within countries in the European Respiratory Health Survey (18). In a recent report (33), there has also been shown significant variations in plasma vitamin C levels, reflecting different dietary antioxidant intake, in subjects with different ethnic backgrounds living in the same area. Further search for determinants of respiratory symptoms should take into account possible differences in total energy intake and dietary items, including vitamin C intake, across the populations at examination.

In conclusion, dietary vitamin C intake appeared to be inversely related to symptoms of “cough” and “wheeze”, indicating that there may be a protective antioxidant effect in young adult smokers.

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