LEVELS OF VITAMIN C IN CHAIN SMOKERS
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Abstract
Introduction: Cigarette smoking induces many chronic illnesses, but in developed countries it is a preventable risk factor. However, by increasing the protective mechanism, it may be possible to alleviate the smoke-induced damage. As smoking risk is minimised by vitamin C intake, it is recommended that smokers should take more vitamin C. This inverse correlation between both vitamin C intake and serum levels and smoking was independent of age, sex, body weight, ethnicity, and consumption of alcoholic beverages. The negative association between cigarette smoking and serum vitamin C levels continued, following further adjustment for dietary vitamin C intake. The risk of severe hypovitaminosis C, especially when not accompanied by vitamin supplementation, has been increased in smokers. These data indicate that the inverse relationship between smoking and serum vitamin C levels exists independently of dietary intake, while smoking adversely affects preferences for vitamin C rich foods.

Methods: A survey method was performed, with 50 smokers (S) receiving either 500 mg of vitamin C or placebo (P) daily for 4 weeks, and 50 non-smokers receiving vitamin C without supplementation. All finished the hearing. Both groups were equal and C: 14.2 + /- 1.8 pack-years was the amount of cigarettes smoked. Concentrations of plasma vitamin C increased significantly (p < 0.005) only in the vitamin C supplement community.

Results: At SMHRC Hospital Nagpur, we examined the relationship between smoking and vitamin C status, dietary and serum vitamin C levels of 100 participants. Smokers of 20 cigarettes a day had the lowest dietary intake of vitamin C and serum levels, whereas smokers of 1-19 cigarettes a day had lower intake of vitamin C and serum levels (compared to respondents who had never smoked. This inverse correlation between vitamin C and smoking intake and serum levels was independent of age, sex, body weight, race, and consumption of alcoholic beverages. The negative association between cigarette smoking and serum vitamin C levels continued, following further adjustment for dietary vitamin C intake. In smokers, the risk of severe hypo-vitaminosis C, particularly when not accompanied by vitamin supplementation, has increased.

Conclusion: These data indicate that the inverse relationship between smoking and serum vitamin C levels exists independently of dietary intake, while smoking adversely affects preferences for vitamin C rich foods. A balanced diet for smokers will obtain a hearty recommendation at this time, but guidelines should remain cautious about high-dose nutrition supplements.

Keywords: Chain Smoker, Vitamin C, hypo-vitaminosis C and cigarette.

Introduction
Preliminary reports have shown adverse effects of smoking on the metabolism of vitamin C (1,2) and more recent studies have confirmed that serum vitamin C levels in cigarette smokers are lower than in non-smokers. (3) These results suggest that smoking directly lowers serum vitamin C levels, although other factors have also been identified, including gender, (4) age, (5) and ethanol intake (6) Since cigarette smoking is not, however, independent of age, sex, or consumption of alcohol. (7) The relationship between smoking and vitamin C status requires assessment for these potentially confusing variables to be monitored. These issues have been partly addressed in many previous studies by stratifying participants by age, sex, and level of vitamin C intake. (8, 9) Vitamin C levels have been decreased in smokers within each stratum, indicating that the relationship may still be independent of these influences.

Extensive epidemiological studies have shown that low fruit and vegetable intake in cigarette smokers is associated with an increased risk of lung cancer. The likelihood of some form of association between nutrients and cigarette smoke is supported by the finding that smokers have lower plasma vitamin C and plasma carotenoid levels than non-smokers, even after adjustment for some. In addition, tobacco smokers have increased whole-body vitamin C turnover. The risk of cardiovascular disease is also significantly increased for smokers; cigarette use is a major contributor to atherosclerosis and stroke. (10) While a portion of the carcinogenic effects of smoke have been attributed to mutational inactivation of the p53 tumour suppressor gene, (11) the relationship mechanisms...
between cigarette smoke and heart disease have only recently begun to explain

Thus, though there seems to be unequivocal evidence supporting the finding that smoking results in lower vitamin C plasma concentrations, the clinical relevance of this depletion remains to be explained, beyond that of scurvy. Studies of the potential beneficial impact of supplementation with antioxidants on smokers have provided unclear results. It should not be ignored, however, that a large proportion of the population in developing countries appears to be suffering from subclinical vitamin C deficiencies, which are likely to affect both short-term and long-term health and could easily be cured. This chapter discusses the clinical significance of smokers’ long-term low vitamin C status and the emerging pros and cons of vitamin C supplementation for smokers.

The goal of this study was to better define the independent relationship between vitamin C status and cigarette smoking.

Methods

Until registration, all participants issued written informed consent. The sample was chosen so that population subgroups of particular interest were oversampled for nutritional evaluation. The oversampled classes of adults included people over 60 years of age and people below the level of poverty. Sample weights for these subgroups were then determined such that the non-institutionalized civilian population was closely estimated in the overall sample. The individual selection likelihood, adjustments for non-response, and post stratification adjustments are expressed in this sample weighting. A full explanation of the methodology of the survey has been reported.(12) Adults 18 to 74 years of age who attended a second review visit after a preliminary interview were studied. However, the study excluded respondents who did not have calculated serum vitamin C concentrations, who did not report alcoholic beverage intake, and who did not complete smoking histories (n=50). 100 respondents remained eligible for the study after these exclusions. In order to compensate for potential non-response bias introduced due to failure to attend the second review visit, sufficient sample weighting was used. (13) Those who attended the second visit but were subsequently excluded (n=50) were comparable in percent who were male, currently smoking, and in their mean age to the included subjects. Nutrient intakes from 24-hour recall interviews have been calculated. Recent intakes of individual food products, including figures for liquor, have been given by three-month food frequency surveys. The query "Are you taking vitamins or supplements?" determined the use of vitamin and mineral supplements. The vitamin content of the supplements was omitted from the summaries of the nutrient intake and thus the measured vitamin C intake underestimates the actual consumption of vitamin C among those respondents taking supplements. For this reason, in the multivariate analysis evaluating serum vitamin C levels, the use of supplements was included as a separate variable.

Serum vitamin C levels were measured in a central laboratory at the Centers for Disease Control (CDC) by the dinitrophenyl hydrazine method.(14) Respondents with serum vitamin C levels of 0.2 mg/dl or less were considered to be at high risk for clinical vitamin C deficiency while those with serum concentrations of 0.4 mg/dl or less were considered to be at marginal risk.

For the complicated sample design, variance estimates were corrected. (15) To assess the independent contribution of a variable to serum vitamin C levels, multiple regression was used while simultaneously controlling for all other variables. (16) The order of entry was determined using a stepwise regression model, but regression coefficients were estimated after all variables were introduced into the model. Smoking status was classified into six levels for the regression equations: never smoked, quit for the previous year or longer, quit in the previous year, smoking less than 20 cigarettes a day, smoking 20 cigarettes a day, and smoking more than 20 cigarettes a day. This was done to compare serum vitamin C levels in cohorts of subjects who were currently smoking, stopped smoking, or stopped smoking. Smoking status was also reported as a continuous variable in additional studies. The Mantel Haenzel method calculated odds ratios for smoking and nutrient supplements on the risk of hypovitaminosis C when adjusting for potential confounding variables. (17,18)

Result

Table 1: Dietary Vitamin C Intake, Serum Vitamin C Levels, and Smoking Frequency in Individuals by Category of Gender, Age Tertiles and Alcohol Consumption.

<table>
<thead>
<tr>
<th>GENDER</th>
<th>N</th>
<th>Smokers (per cent)</th>
</tr>
</thead>
<tbody>
<tr>
<td>Male</td>
<td>50</td>
<td>10.6%</td>
</tr>
<tr>
<td>Female</td>
<td>50</td>
<td>4.8%</td>
</tr>
<tr>
<td>Age (years)</td>
<td></td>
<td></td>
</tr>
<tr>
<td>18-35</td>
<td>45</td>
<td>10.9%</td>
</tr>
<tr>
<td>36-59</td>
<td>35</td>
<td>7.2%</td>
</tr>
<tr>
<td>60-74</td>
<td>20</td>
<td>5.4%</td>
</tr>
<tr>
<td>Alcohol (drinks/weekly)</td>
<td></td>
<td></td>
</tr>
<tr>
<td>None</td>
<td>30</td>
<td>2.5%</td>
</tr>
<tr>
<td>1-5</td>
<td>48</td>
<td>6.5%</td>
</tr>
<tr>
<td>&gt;5</td>
<td>22</td>
<td>10%</td>
</tr>
</tbody>
</table>

Univariate tests for variables correlated with both serum vitamin C levels and the prevalence of cigarette smoking are shown in Table 1. Sex, race, age, and body mass index were significantly associated with serum vitamin C levels. Males, relative to females and adults under the age of 60,
had lower serum vitamin C levels and a higher incidence of smoking compared to those over 60. On the other hand, heavier individuals had lower serum vitamin C concentrations and a lower smoking prevalence. A greater probability of smoking was associated with higher ethanol intakes, while a non-significant rise in vitamin C levels was observed in those with more modest intakes.

Smokers had serum vitamin C levels that were 24 percent lower than non-smokers, in addition to reduced vitamin C intake. The lowest serum vitamin C concentrations were observed in smokers of 20 cigarettes a day, while serum vitamin C levels were highest in individuals who had either quit smoking for more than one year or who had never smoked. Even after correcting for variations in dietary intake, age, gender, body weight, and vitamin supplementation, the decrease in serum vitamin C levels observed in smokers persisted. Smoking status was the most significant non-nutritional predictor of serum vitamin C levels in a multiple regression study, explaining more of the total variance than gender or age. Smoking status was entered into the regression equation as a continuous variable defined as the amount of cigarettes smoked daily in additional analyses.

Table 2: Effect of Smoking Status on Dietary Vitamin C Intake

<table>
<thead>
<tr>
<th>Smoker</th>
<th>N</th>
<th>Dietary Vitamin Intake (mg) Mean</th>
</tr>
</thead>
<tbody>
<tr>
<td>Smoker</td>
<td></td>
<td></td>
</tr>
<tr>
<td>&gt;1 PPD</td>
<td>38</td>
<td>9.3</td>
</tr>
<tr>
<td>1 PPD</td>
<td>22</td>
<td>7.4</td>
</tr>
<tr>
<td>&lt;1 PPD</td>
<td>40</td>
<td>11.2</td>
</tr>
<tr>
<td>Non-smoker</td>
<td></td>
<td></td>
</tr>
<tr>
<td>DC &lt; 1 yr</td>
<td>20</td>
<td>6.6</td>
</tr>
<tr>
<td>DC &gt; 1 yr</td>
<td>30</td>
<td>8.7</td>
</tr>
<tr>
<td>Never smoked</td>
<td>50</td>
<td>13.5</td>
</tr>
</tbody>
</table>

**NOTES:** >1 PPD-Greater than 1 pack per day; 1 PPD-One pack per day; <1 PPDL less than one pack per day; DC < 1 yr-Stopped smoking within the past year; DC > 1 yr-Stopped for the previous year or longer. *Mean vitamin C intake adjusted for age, sex, race, ethanol intake, monetary income, and body weight.

Table 2 indicates an inverse association between cigarette smoking and the consumption of dietary vitamin C. Compared with non-smokers, the mean consumption of vitamin C for all smokers was 20 percent lower. This decrease was particularly noticeable in people who smoke 20 cigarettes daily. Smokers with fewer than 20 cigarettes a day had an intermediate intake of vitamin C, whereas people who quit smoking for more than a year had an intake of vitamin C equivalent to never-smokers. After adjustment for age, sex, race, ethanol consumption, income and body weight, this inverse relationship between smoking and dietary vitamin C consumption persisted.

The incidence of low serum vitamin C levels occurring in smokers was compared to that of non-smokers in order to test the hypothesis that smoking raises the risk of hypovitaminosis C. Of all smokers, 7.4% had serum levels of vitamin C of 0.2 mg/dl or less, compared with 1.9% of non-smokers who had equivalent levels of vitamin C. An additional 19.7% of smokers, compared to 8.2% of non-smokers, had serum vitamin C levels between 0.2 mg/dl and 0.4 mg/dl. Since the mean serum vitamin C levels were not affected by further adjustment for BMI and age, only gender and dietary vitamin C intake were used as control variables to assess smoking risk for marginal or serious hypovitaminosis C. After gender and dietary modification, smoking risk ratios of 3.5 for extreme 3.1 for marginal hypovitaminosis C were obtained. A small reduction in the odds ratio resulted in further modification for dietary vitamin C intake. Of the total study, 37 percent reported taking supplements with vitamins or minerals. Dependent on smoking and supplementation, the incidence of marginal hypovitaminosis C.

**Discussion**

Our review of the SMHRC Hospital Nagpur data confirms that decreased serum vitamin C levels are correlated with cigarette smoking. Despite correction of variables that independently affected serum vitamin C levels, such as age, gender, ethnicity, and BMI, this association persisted. In smokers, dietary vitamin C intake was lower than in non-smokers, a result that may theoretically explain this inverse association. Further adjustment for vitamin C consumption, however, showed that the relationship between smoking and serum levels was independent of dietary intake. In fact, smoking status clarified more than the self-reported dietary intake of vitamin C, the overall variance of serum vitamin C levels. In addition, there was no major reduction in the increased risk of hypovitaminosis C in smokers while controlling for reduced dietary vitamin C intake associated with smoking. These results indicate that cigarette smoking has a substantial effect on the levels of serum vitamin C, which occurs mainly through a mechanism independent of reduced dietary vitamin C intake.

There have been previously documented inverse associations between smoking and vitamin C status. However, most studies used small sample sizes (3,8) or were unable to monitor potentially misleading variables. (7,8) Pelletier stratified and evaluated 4,500 Canadians participating in the National Survey of Nutrition Canada into three groups of dietary vitamin C intake, Gender and age-based serum vitamin C levels; an average 30% decrease in serum levels was observed in smokers compared with non-smokers. (8) Ritzel, et al, calculated that mean serum vitamin C levels in 4,053 healthy Swiss
employees were lower in smokers, independent of weekly citrus fruit intake. (9) The risk of extreme or marginal hypovitaminosis C in smokers was approximately three times higher.

In smokers, the decreased serum vitamin C levels may be due to either impaired absorption of vitamin C or increased turnover. Kallner, et al, used radio-labelled ascorbic acid to test vitamin C kinetics and showed increased turnover in smokers but only minor differences in absorption relative to non-smokers. (19) Others have stated that smoking acutely improves vitamin C urinary excretion, (20) which also suggests an accelerated metabolism in smokers. Interactions between the metabolism of vitamin C and a number of drugs have been described.(21,22) Further research will be needed to identify the responsible compound in tobacco smoke and to establish its mechanism.

In this study, serum vitamin C levels, independent of dietary vitamin C intake, were approximately 0.2 mg / dl lower in smokers compared with non-smokers. Therefore, the effect of smoking on the reduction of serum vitamin C levels in participants with initially low serum vitamin C levels was proportionately greater. For extreme or minimal hypovitaminosis C, this resulted in a higher proportion of smokers with serum levels below the 0.2 mg / dl range cutoff. In this aspect, relative to non-smokers, the risk ratio for hypovitaminosis C was threefold higher in smokers. Therefore, while the prevalence of extreme and marginal hypovitaminosis C was low, certain subgroups might be at greater risk, such as smokers not taking nutritional supplements.

The observed decrease in dietary vitamin C intake was unexpected among smokers. While altered food preferences have been identified in smokers compared to non-smokers,(23,24) a particular association between smoking and vitamin C intake is not well recognised. Our finding that the intake of vitamin C was lowest in people who smoke 20 cigarettes or more daily, and that smokers who have quit for more than one year have intakes comparable to people who have never smoked, indicates that smoking has a particular aversive impact on vitamin C rich foods that could be reversible if smoking is quit.

While it was determined that an association between depressed vitamin C levels and smoking was independent of other potentially influencing factors, it is not possible to conclude a cause and effect relationship from this research. Prospective research would be needed both to show that smoking has a direct impact on the metabolism of vitamin C and to examine potential mechanisms. However, there were lower mean serum vitamin C levels in the cohort of participants who smoked less than 20 cigarettes daily than heavier smokers but higher than non-smokers, indicating a dose-response effect. Moreover, former smokers had higher serum levels than current smokers, suggesting that the effect of smoking could be reversible on serum vitamin C levels. These findings indicate that the correlation of vitamin C levels between smoking and serum may be causal.

Conclusion
The least likely to eat them are those probably in need of vitamin C supplements. The largest subpopulation that will theoretically benefit from vitamin C supplementation is smokers who actually do not take supplements because a substantial proportion remain at elevated risk of vitamin C deficiency due to poor eating patterns and tremendous voluntary exposure to oxidants. A significantly reduced risk of suffering from scurvy-like symptoms, including exhaustion, fatigue, and depression, can be a possible short-term gain from such supplementation. Only large controlled clinical trials will determine whether there is a long-term advantage in terms of the lower occurrence of cardiovascular disease and cancers. It is therefore critical that future research concentrate on people who have a low daily intake of vitamin C. Regulated trials are required to better explain the long-term implications for these particular individuals with low vitamin C status in both smokers and the general population, as well as the clinical effects with moderate vitamin C supplementation. For a large part of the population, there seems to be a fair possibility of a value-for money health benefit.

References
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