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Serum vitamin C–periodontal relationship in community-dwelling elderly Japanese

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Abstract

Objective: To determine the relationship between serum vitamin C and periodontitis as estimated by clinical attachment loss (CAL) in community-dwelling elderly Japanese.

Material and Methods: This analysis was confined to 413 Niigata citizens aged 70 years in whom the data for serum vitamin C and CAL were available. High-pressure liquid chromatography method was used to ascertain the serum vitamin C levels while CAL was assessed on six sites of all teeth present including third molars by means of pressure-sensitive probes. Other variables included gender, smoking, toothbrushing frequency, number of teeth present and random blood sugar levels.

Results: Serum vitamin C concentration was inversely related to CAL ($r = -0.23$, $p < 0.00005$) at bivariate level. Multiple linear regression analysis showed that CAL was 4% greater in subjects with lower serum vitamin C levels than in subjects with higher serum vitamin C levels notwithstanding smoking, diabetes, oral hygiene, gender or number of teeth present.

Conclusion: The findings suggested that serum vitamin C might have relatively weak but a statistically significant relationship with periodontitis in this elderly population.

Key words: elderly; periodontitis; serum vitamin C

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Investigations into vitamin C (ascorbate/ascorbic acid)–periodontal relationship go as far back as the 18th century when a British naval physician revealed that scurvy, which was accompanied by putrid gums could be successfully treated with oranges and lemons (Rubinoff et al. 1989). Since then numerous experimental as well as epidemiological studies in both humans and animals have attempted to address this issue but the findings have been rather incoherent: some have failed to suggest any significant relationship between vitamin C and periodontal disease (Waerhaug 1958, Barros & Witkop 1963, Russel et al. 1965, Enwonwu & Edozien 1970, Woolfe et al. 1980, 1984) while others reported that the deficiency of this vitamin could not be correlated with severe periodontitis but with gingival inflammation or acute necrotizing ulcerative gingivitis (Enwonwu 1972, Shannon 1973, Leggott et al. 1986, Melnick et al. 1988). Still others have observed a weak association between vitamin C and periodontitis (Ismail et al. 1983, Nishida et al. 2000). However, the majority of workers who have looked into ascorbic acid–periodontal relationships in humans estimated the dietary intake of vitamin C (Ismail et al. 1983, Nishida et al. 2000) in comparison to the few who have assessed serum or plasma ascorbic acid levels (Leggott et al. 1986, Melnick et al. 1988, Pussinen et al. 2003), which might provide much reliable information than the former method (Simon & Hudes 2001). On the other hand, little or virtually nothing has been reported in the literature on the association between vitamin C and periodontal status of the elderly who may be at a higher risk of developing vitamin C deficiency compared with other age groups (Rubinoff et al. 1989, Pussinen et al. 2003). In view of these facts, it is important to explore the link between serum ascorbic acid levels and periodontitis in an elderly population. Accordingly, the main purpose of the present investigation was to ascertain the relationship between serum vitamin C levels and periodontitis as measured by clinical attachment loss (CAL) among senior citizens in Japan.

Material and Methods

This was a part of the ongoing oral and general health survey, which has been carried out in senior citizens of Niigata city, Japan since 1998. The study methodology has been described in

detail elsewhere (Hirotomi et al. 2002, Ogawa et al. 2002). A written invitation was sent to all individuals aged 70 years ($n = 4542$; 2099 males and 2443 females) who were registered as the citizens of Niigata city, Japan in 1998 to take part in this survey once the Ethical Committee of the School of Dentistry, Niigata University, approved the research protocol of the survey. After sending a second request, 79.5% (3695) of the population consented to participate in the survey. Having considered the resources available, out of the positive respondents 600 individuals were randomly recruited into a cross-sectional community-based study so as to have an approximately equal number of males (306) and females (294). Informed consent was obtained from all subjects prior to the investigation.

Four calibrated dentists conducted the intra-oral examination involving assessment of CAL, probing depth (PD) and bleeding on probing (BOP) using mouth mirrors and pressure-sensitive TPS Probe® (Vivacare, Schaan, Liechtenstein) under artificial light. All teeth present including third molars were probed at six sites per tooth, namely, mesio-buccal, mid-buccal, disto-buccal, disto-lingual, mid-lingual and mesio-lingual and the recordings were rounded up to the nearest whole millimetre. Calibration of the examiners was carried out before and during the survey and the examiner consistency ranged from 0.56 to 0.92 as indicated by κ statistic. Information pertaining to smoking habits as well as oral hygiene practices was obtained by means of a personal interview, whereas blood samples were sent to the laboratory in order to evaluate the serum vitamin C levels using high-pressure liquid chromatography (HPLC) method and random blood sugar levels.

Statistical analyses were carried out by means of STATA statistical software package. Throughout the analysis, CAL, the dependent variable, was considered as a continuous variable and the unit of analysis was the subject. Among independent variables, serum vitamin C level was a continuous variable while gender (male:female), smoking status (current smoker: ex-smoker: non-smoker), diabetic status (random blood sugar (RBS) < 140 mg/dl: $\geqslant 140$ mg/dl), frequency of tooth cleaning (< 2/day: $\geqslant 2$/day) and the number of teeth present (< 20 teeth: $\geqslant 20$ teeth) were treated as categorical variables. To compare the difference between two means Student's *t*-test was employed while one-way ANOVA combined with Bonferroni's test was used where necessary to compare more than two means. Moreover, the association between two continuous variables was determined by means of Pearson's correlation technique. Finally, having excluded the presence of multicolinearity, the independent variables that showed significant relationships with CAL at bivariate level were included in a multiple linear regression analysis to identify the independent effect of serum vitamin C level on CAL while controlling for other confounding factors. The level of statistical significance was fixed at $p \leqslant 0.05$.

Results

The current analysis was limited to 413 dentate subjects in whom the data for CAL as well as serum concentrations of vitamin C were available. The serum levels of vitamin C ranged from 0.2 to 22.6 mg/l with a mean of 7.21 (results not shown). Table 1 shows the periodontal characteristics of the sample. Accordingly, the mean CAL was 3.26 mm (SD = 1.05) while the mean PD was 2.1 mm (SD = 0.58). The mean percentage of BOP per person was 7.3 (SD = 8.6). It was also observed that 62.6% of subjects had at least one site with CAL of $\geqslant 6$ mm, whereas almost one-third (33%) of the sample exhibited PD of $\geqslant 6$ mm at least on one site (results not shown). Indeed, there was no significant relationship between serum vitamin C levels and either PD or BOP (results not shown) and consequently, it was decided to confine the present analysis to explore the relation between the independent variables including serum vitamin C concentration and CAL. Table 2 depicts the associations between CAL and the independent variables including gender, smoking status, diabetic status, brushing frequency, the number of teeth present and serum vitamin C concentrations. As revealed by Student's *t*-test, males had significantly greater CAL (mean = 3.54 mm; SD = 1.2) than females (mean = 2.96 mm; SD = 0.8 mm) while those who had 20 or more teeth showed significantly lower CAL (mean = 2.92 mm; SD = 0.8) compared with the subjects with < 20 teeth (mean = 3.69 mm; SD = 1.2). It is also apparent that CAL was significantly higher in the

Table 1. Periodontal characteristics of the sample

Variable	Mean	SD
CAL (mm)	3.26	1.05
PD (mm)	2.10	0.58
BOP (%)	7.30	8.60

CAL, clinical attachment loss; PD, probing depth; BOP, bleeding on probing

Table 2. Relationships between CAL and independent variables at bivariate level

Independent variables	CAL Mean (SD)	*p*
Gender*		
male ($n = 215$)	3.54 (1.2)	< 0.00005
female ($n = 198$)	2.96 (0.8)	
Number of teeth present*		
< 20 ($n = 184$)	3.69 (1.2)	< 0.00005
$\geqslant 20$ ($n = 229$)	2.92 (0.8)	
Brushing frequency*		
< 2/day ($n = 145$)	3.40 (1.1)	< 0.05
$\geqslant 2$/day ($n = 268$)	3.20 (1.0)	
Smoking status†		
current smoker ($n = 71$)	3.82 (1.3)	< 0.00005‡
ex-smoker ($n = 137$)	3.45 (1.1)	
non-smoker ($n = 205$)	2.95 (0.8)	
Diabetic status*		
RBS < 140mg/dL (n = 356)	3.22 (0.1)	< 0.05
RBS $\geqslant 140$ mg/dl ($n = 57$)	3.52 (0.2)	
Serum ascorbic acid§	$r = -0.23$	< 0.00005

CAL, clinical attachment loss; RBS, random blood sugar. *Student's *t*-test.
†One-way ANOVA.
‡Bonferroni's test: $3.82 > 3.45 > 2.95$ ($p < 0.05$).
§Pearson's correlation.

Table 3. Multiple linear regression model for CAL with significant variables

Independent variables	Coefficient	SE	*p*	95% CI	
Serum ascorbic acid	− 0.04	0.02	< 0.05	− 0.06	− 0.005
Current smoker	0.57	0.17	< 0.005	0.24	0.92
Gender (male = 0)	− 0.30	0.04	< 0.05	− 0.58	− 0.01
Teeth present (< 20 = 0)	− 0.73	0.09	< 0.0005	− 0.92	− 0.55
Constant	3.83	0.25	< 0.0005	3.46	4.20

$R^2 = 0.26$; $p < 0.00005$; SE, standard error; CI, confidence interval.

subjects who brushed their teeth < 2/day than in those who used a toothbrush ⩾ 2/day. One-way ANOVA combined with Bonferroni's post hoc test disclosed that current smokers had significantly worse CAL (mean = 3.82 mm; SD = 1.3) in comparison with both ex-smokers (mean = 3.45 mm; SD = 1.1) and non-smokers (mean = 2.95 mm; SD = 0.8), whereas subjects with RBS < 140 mg/dl showed significantly lower CAL than those who had RBS ⩾ 140 mg/dl. Furthermore, there was an inverse relationship between serum vitamin C concentration and CAL as indicated by Pearson's correlation technique ($r = -0.23$; $p < 0.00005$).

All the independent variables that demonstrated significant effects on CAL at bivariate level, namely, serum vitamin C, smoking status, diabetic status, gender, toothbrushing frequency and the number of teeth present were included in a multiple linear regression analysis and the variables that remained significant in the final model are shown in Table 3. Accordingly, it was found that serum vitamin C had a significant effect on CAL (correlation coefficient = − 0.04; $p < 0.05$), which was independent of the other covariates including smoking and random blood sugar levels. The independent variables in the final model explained 26% of the variance in CAL ($R^2 = 0.26$).

Discussion

The findings of this cross-sectional study suggested that there was a weak but significant association between the level of serum vitamin C and periodontitis as measured by CAL notwithstanding the effect of established risk factors for periodontitis such as smoking and diabetes mellitus in this elderly population. In other words, we observed an inverse independent relationship between serum vitamin C concentration and CAL – the lower the level of serum vitamin C the higher was the periodontal attachment loss. This was indicated by the relatively smaller correlation coefficient of serum vitamin C (correlation coefficient = − 0.04): CAL in subjects with lower serum vitamin C levels would only be 4% greater compared with those who had higher serum vitamin C concentrations regardless of other covariates.

Notwithstanding the fact that our study was confined only to the elderly and that we evaluated serum ascorbic acid concentration instead of dietary intake of vitamin C, the present findings may be comparable to those of others (Ismail et al. 1983; Nishida et al. 2000) who observed a weak albeit statistically significant relationship between dietary vitamin C and periodontal disease in the US adults. In particular, the latter (Nishida et al. 2000) found that even after controlling for the effects of age, gender, smoking and gingival bleeding, the level of periodontitis in subjects with a lower dietary intake of vitamin C was 1.19 times greater than that of individuals with a higher intake of vitamin C while the former (Ismail et al. 1983) did not adjust for such factors. More recently, Pussinen et al. (2003) who investigated the relation between plasma vitamin C levels and serology of periodontitis in Finnish and Russian men observed that the antibody levels to *Porphyromonas gingivalis* were inversely correlated with plasma vitamin C concentrations ($r = -0.22$; $p < 0.001$) and this association remained significant in a linear regression model even after controlling for confounding factors. Accordingly, they concluded that lower concentrations of plasma vitamin C might increase the risk of periodontitis, which is in accord with the present findings.

Various researchers have proposed several plausible biological mechanisms while attempting to explain how ascorbic acid could affect the healthy tissues in humans as well as in animals (Goetzl et al. 1974, Alfano et al. 1975, Boxer et al. 1979, Dallegri et al. 1980, Alvares et al. 1981, Alvares and Siegel 1981, Berg et al. 1983, Leggot et al. 1986, Jacob et al. 1987, Nakamoto et al. 1984). It has been established that ascorbic acid plays a major role in the synthesis of collagen, especially the hydroxylation process, helix formation and cross-linking of collagen molecules (Alfano et al. 1975, Berg et al. 1983). Collagen is undoubtedly an essential component of human tissues including periodontium and required in wound healing as well as periodontal regeneration and maintaining the integrity of the gingival vasculature. Also, there are several lines of evidence to suggest that vitamin C affects chemotaxis as well as phagocytosis of polymorphonuclear leucocytes and thereby influences the host-immune reactions (Alfano et al. 1975, Boxer et al. 1979, Dallegri et al. 1980, Patrone et al. 1982). Moreover, some researchers have hypothesized that ascorbic acid might express an antihistamine effect through direct detoxification of histamine or indirectly affecting the histamine breakdown and this in turn would retard gingival inflammation (Nakamoto et al. 1984) whereas others (Alfano et al. 1975, Alvares and Siegel 1981) reported that the deficiency in vitamin C levels could be linked to increased permeability of gingival mucosa, which allows easy passage of microbial and other noxious products into the periodontium. It has also been shown that ascorbic acid demonstrates antioxidant properties and therefore is considered one of the constituents of antioxidant defence mechanism in human body (Nishida et al. 2000). Tobacco, especially, cigarette smoke contains various oxidants that cause tissue damage and consequently smokers do require a higher serum concentration of vitamin C than non-smokers do (Kallner et al. 1981, Nishida et al. 2000). Moreover, given that avitaminosis C and diabetes mellitus share some common pathological characteristics such as raising of oxidant stress (Schmidt et al. 1996) and collagen degradation (Kjersem et al. 1988) in gingival tissues, it has been hypothesized that vitamin C might play a critical role in the aetiology and/or progression of periodontitis in type I diabetics (Aleo 1981, Nishida et al. 2000). In this connection, it is also noteworthy that both diabetes as well as smoking, which are regarded as well-established risk factors for periodontitis, may contribute to oxidative tissue damage and given the antioxidant properties

of vitamin C, it might act as a potential moderator in both smoking– and diabetes–periodontal relationships – this would be an interesting hypothesis to be tested in future investigations. Although exploring such biological mechanisms and/or hypotheses was beyond the scope of our study, the association between serum vitamin C levels and CAL that was observed even after controlling for known risk factors such as smoking and diabetes mellitus in the present study could be explained on the basis of these mechanisms. This is further augmented by the fact that such mechanisms could be connected to pathogenesis of periodontal disease, which is of inflammatory nature and which may be mediated through the tissue damage caused by interaction of microbial noxious products and host-immune response. However, it should also be highlighted that the observed relationship is rather weak and that these biological phenomena involving vitamin C have neither been clearly understood nor well defined (Leggot et al. 1986, Nishida et al. 2000, Pussinen et al. 2003).

This study population comprised non-institutionalized elderly people who were active, living independently and willing to participate in the survey. It has been shown that the elderly who are institutionalized, less active and dependent are at a higher risk for periodontal disease than those who are active and independent (Hirotomi et al. 2002, Ogawa et al. 2002). Besides, the mean serum concentration of vitamin C in this sample was rather high and the serum vitamin C level in only about 4% of subjects (results not shown) was below the reference range for Japanese elderly (Sakai et al. 1998). In this context, the current sample might be considered a biased one and therefore the findings should be interpreted with caution.

In conclusion, the results suggest that the serum vitamin C levels in this elderly population weakly correlate with periodontitis as evaluated by CAL notwithstanding the effects of smoking, diabetes mellitus, gender, oral hygiene practices or the number of teeth present. Moreover, considering the cross-sectional nature of the study design it was almost impossible for us to ascertain lifetime changes in either the vitamin C intake or serum vitamin C levels in this population. Because of these facts and also given the relatively low correlation observed between serum vitamin C and CAL in the current analysis, we could neither confirm an unambiguous cause–effect relationship between serum vitamin C and periodontitis nor a substantial beneficial effect of vitamin C on periodontal health. All in all, the association observed here could not be a straightforward one but it would be plausible that the serum vitamin C might be inflicting a moderating influence on periodontitis through the established risk factors such as smoking and diabetes, as it was mentioned hitherto. Consequently, it warrants further investigations, in particular, longitudinal studies and experimental designs to explore the actual role of vitamin C in the aetiology and/or progression of periodontal disease. It should also be highlighted that this elderly cohort will be followed up for several years and thus, we intend to analyse the serum vitamin C–periodontal relationship prospectively, in the same population.

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