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Ⅳ．研究成果の刊行物・別刷

口腔保健と全身の QOL の関係に関する総合研究

（H20－循環器等（歯）－一般 －002）

The Relationship Between Serum Lipids and Periodontitis in Elderly Non-Smokers

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Background: There are common risk factors for periodontal disease and cardiovascular disease in elderly patients. Some studies reported that a low total cholesterol (TC) serum level is associated with a higher level of death in the elderly. The purpose of this study was to investigate the relationship between serum lipids and periodontal disease in non-smoking elderly patients.

Methods: Two hundred thirty-four non-smokers (63 males and 171 females) participated in this study. Multiple regression analysis was performed to evaluate the relationship between serum lipids and periodontitis and between serum lipids and inflammatory factors. The percentage of sites with probing depth (PD) ≥4 mm, clinical attachment level (CAL) ≥4 mm, and bleeding on probing (BOP) were used as dependent variables. TC, high-density lipoprotein cholesterol (HDL-C), gender, and the number of teeth present were included in the model as independent variables in the first analysis. TC, HDL-C, and low-density lipoprotein cholesterol (LDL-C) were used as dependent variables. Albumin, inorganic phosphorus, calcium, and C-reactive protein were used as independent variables in the second analysis.

Results: According to the results of the multiple linear regression analysis, TC was associated with the percentage of sites with PD ≥4 mm (P <0.01; β = −0.19), CAL ≥4 mm (P<0.01; β = −0.20), and BOP (P= 0.03; β = −0.16). HDL-C and LDL-C have a significant association with inflammatory markers and inorganic phosphorus and calcium, respectively.

Conclusion: Higher TC is associated with a lower prevalence of periodontitis in non-smoking elderly patients. *J Periodontol 2009;80:740-748.*

KEY WORDS

Cholesterol; elderly; periodontal disease.

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Studies[1,2] have reported that high serum total cholesterol (TC) or low-density lipoprotein cholesterol (LDL-C) is a risk factor for new or recurrent coronary heart disease in the general population. In addition, associations between periodontal disease and general health conditions, such as coronary heart disease, were recently reported.[3-7] Chronic low-grade inflammations, such as periodontal disease, are suggested to be associated with the onset and progression of cardiovascular disease.

There are common risk factors for periodontal disease and cardiovascular disease in elderly patients. Serum lipids might be the most important of these factors. Reduced high-density lipoprotein cholesterol (HDL-C) levels are well-recognized risk factors for cardiovascular disease and ischemic stroke.[4,6] Moreover, two cross-sectional epidemiologic surveys[7,8] have been conducted in Japan to assess the associations between blood chemistry variables and periodontal status. One study[7] concluded that periodontal disease was common in the subjects with low serum concentrations of HDL-C (<60 mg/dl). The other study[8] concluded that neither TC nor triglycerides (TGs) were associated with periodontal disease, but HDL-C was related to a lower risk for periodontal disease. The results of both studies indicated that elevated HDL-C levels were correlated with lower levels of periodontal disease.

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According to Katz et al.,[9] hypercholesterolemia and cardiovascular diseases are related to periodontal disease.

However, some studies[10-14] reported that a low serum level of TC is associated with greater mortality. In older persons, it was shown to have a U- or J-shaped relationship, to be inversely related, or not to be related to the risk for death.[15,16] One possible explanation for this phenomenon is selective mortality, based on the hypothesis that many individuals with high levels of serum lipids had already died and were not included in the sample. In this situation, those with higher TC might experience an earlier onset of severe cardiovascular disease, leading to a disproportionately greater mortality before study enrollment. Based on these results, it is possible to hypothesize that the relationship between serum lipids and periodontal disease might be changeable in the elderly. In addition, smoking is known to be an effect modifier in periodontal disease.[17] Therefore, a relationship between serum lipids and periodontal disease might only exist among non-smokers.

In view of these factors, the purpose of this study was to investigate the relationship between serum lipids and periodontal disease in non-smoking elderly patients.

MATERIALS AND METHODS

Study Population

In 1998, a written invitation to participate in this survey, in which the aim of the present study was briefly described, was mailed to all residents (2,099 males and 2,443 females) in Niigata City, Japan who were born in 1927. After two requests, 81.4% (n = 3,695) responded positively. The final study sample (n = 600) was randomly selected to have an approximately equal number of males (n = 306) and females (n = 294). None of the subjects were hospitalized or institutionalized. They were in good general health and did not require special assistance with their daily activities. All subjects agreed and signed informed consent forms regarding the protocol, which was reviewed and approved by the Ethics Committee of the Faculty of Dentistry, Niigata University. Those 600 subjects aged 70 years were invited for a follow-up examination, and 355 (200 males and 155 females) subjects were examined in 2006. For analysis, we excluded 121 subjects who were smokers and edentulous. All subjects were examined at local community centers in Niigata City.

Clinical Procedures

Periodontal examination was carried out by four trained dentists under sufficient illumination using artificial light. The periodontal condition, measured as the loss of periodontal attachment in millimeters, was recorded using dental mirrors and specially designed periodontal probes.† Probing was performed at six sites per tooth (mesio-buccal, mid-buccal, disto-buccal, mesio-lingual, mid-lingual, and disto-lingual) for all teeth, including the third molars. Measurements were rounded to the nearest whole millimeter for probing depth (PD) and clinical attachment level (CAL). Bleeding on probing (BOP) and the number of teeth present were investigated. The severity of periodontal disease was defined as the percentage of sites with PD ≥4 mm and the percentage of sites with CAL ≥4 mm. A personal interview was conducted to obtain information regarding gender and smoking habits. Anthropometric evaluation included measurements of weight and height for the calculation of body mass index (BMI). In addition, biochemical values, i.e., total protein, calcium, TC, C-reactive protein (CRP), HDL-C, LDL-C, immunoglobulin G (IgG), inorganic phosphorus, gamma-glutamyl transpeptidase (γ-GPT), and albumin, were measured under non-fasting conditions.

Statistical Analysis

We selected 234 of the 355 subjects (63 males and 171 females) for participation in this analysis because they had one or more teeth and were non-smokers. Initially, we compared the periodontal status, alcohol intake, BMI, serum markers, number of teeth, use of interdental brushes or dental floss, and having had a dental check-up within the last year between males and females. Second, the relationship between periodontal disease and serum lipid variables, including the number of teeth, BMI, use of interdental brushes or dental floss, and having had a dental check-up within the last year were evaluated using Pearson correlation coefficients. Third, a multiple linear regression analysis was used to estimate the independent effect of serum lipids while controlling for confounding factors. Serum lipids were used as the dependent variable, whereas those that showed significant relationships ($P < 0.1$) with periodontal status in the second analysis were selected as independent variables. Fourth, Pearson correlation coefficients were used again to evaluate the correlations between serum lipids and inflammatory and nutritional factors. Finally, a multiple linear regression analysis was used to estimate the independent effect of serum lipids while controlling for confounding factors. Serum lipids were used as the dependent variable, whereas those that showed significant relationships ($P < 0.1$) with periodontal status in the second analysis were selected as independent variables. All calculations and statistical analyses were performed using a statistical software‡ package.

† Vivacare TPS Probe A, Vivacare, Schaan, Liechtenstein.
‡ Stata statistical software, version 6.0, Stata, College Station, TX.

RESULTS

As determined by replicate examinations in 10 patients, the percentage agreement (within ± 1 mm) ranged from 87.5% to 100% for PD and from 83.3% to 100% for CAL. The kappa value ranged from 0.81 to 1.00 for PD and from 0.74 to 1.00 for CAL.

The characteristics of the subjects are shown in Table 1. The mean ± SD for TC was 196.3 ± 29.8 mg/dl for men and 205.7 ± 27.5 mg/dl for women ($P = 0.02$). The mean ± SD for inorganic phosphorus was 3.6 ± 0.6 mg/dl for men and 3.9 ± 0.5 mg/dl for women ($P < 0.01$). Both were higher in females.

Table 1.

Characteristics of Subjects

	Males		Females		
Clinical Characteristic	Mean	SD (n)	Mean	SD (n)	*P* Value
Sites with PD ≥4 mm (%)	11.6	9.8 (63)	9.9	13.6 (171)	0.36
Sites with CAL ≥4 mm (%)	33.9	24.0 (63)	27.7	24.7 (171)	0.09
Sites with BOP (%)	8.1	10.5 (63)	9.1	10.6 (171)	0.50
Teeth present (n)	19.6	8.1 (64)	17.2	8.4 (171)	0.05
BMI (kg/m^2)	22.3	2.4 (63)	22.4	3.34 (166)	0.89
TC (mg/dl)	196.3	29.8 (64)	205.7	27.5 (171)	0.02
HDL-C (mg/dl)	57.7	15.9 (64)	60.9	14.9 (171)	0.16
LDL-C (mg/dl)	111.0	24.1 (64)	116.9	24.1 (171)	0.09
Albumin (g/dl)	4.1	0.3 (63)	4.2	0.3 (171)	0.10
Inorganic phosphorus (mg/dl)	3.6	0.6 (63)	3.9	0.5 (171)	<0.01
Calcium (mg/dl)	9.0	0.4 (63)	9.1	0.4 (171)	0.26
IgG (mg/dl)	1,337.8	264.4 (63)	1,310.7	294.5 (171)	0.52
CRP (mg/dl)*	0.2	0.5 (48)	0.1	0.1 (137)	0.05
γ-GPT (U/l)	22.6	10.3 (64)	24.1	19.0 (171)	0.57
Alcohol intake (n)					
None	31		132		
Sometimes	14		29		<0.01
Every day	18		9		
Unknown	0		1		
Used interdental brushes or dental floss (n)					
Yes	24		75		0.14
No	36		71		
Unknown	3		25		
Had dental check-up within last year (n)					
Yes	50		108		0.02
No	12		60		
Unknown	1		3		

* Sixteen males and 34 females were excluded because of detection-sensitivity limits.

Table 2.

Pearson Correlation Coefficients and *P* Values Between Periodontal Disease and Serum Lipids

Variable	Percentage of Sites With PD ≥4 mm	Percentage of Sites With CAL ≥4 mm	Percentage of Sites With BOP	TC	HDL-C	LDL-C	Gender	Alcohol Intake	Number of Teeth	BMI	Use of Interdental Brushes or Dental Floss	Dental Check-Up Within Last Year
Percentage of sites with PD ≥4 mm												
r	1.00											
P value	–											
Percentage of sites with CAL ≥4 mm												
r	0.63	1.00										
P value	<0.01	–										
Percentage of sites with BOP												
r	0.46	0.27	1.00									
P value	<0.01	<0.01	–									
TC												
r	–0.17	–0.18	–0.20	1.00								
P value	0.01	0.01	<0.01	–								
HDL-C												
r	–0.05	–0.14	–0.17	0.33	1.00							
P value	0.44	0.03	0.01	<0.01	–							
LDL-C												
r	–0.09	–0.08	–0.09	0.83	–0.06	1.00						
P value	0.15	0.25	0.17	<0.01	0.36	–						
Gender (0 = male; 1 = female)												
r	–0.06	–0.11	0.05	0.14	0.10	0.10	1.00					
P value	0.34	0.08	0.46	0.03	0.12	0.13	–					
Alcohol intake (0 = not every day; 1 = every day)												
r	–0.08	–0.11	0.01	0.09	–0.06	0.12	0.28	1.00				
P value	0.20	0.10	0.94	0.19	0.39	0.08	<0.01	–				
Number of teeth												
r	–0.24	–0.48	–0.04	–0.04	0.08	–0.07	0.12	–0.08	1.00			
P value	<0.01	<0.01	0.53	0.52	0.25	0.28	0.07	0.25	–			
BMI												
r	0.10	–0.03	0.03	0.02	–0.24	0.14	0.01	0.05	–0.04	1.00		
P value	0.14	0.69	0.65	0.80	<0.01	0.04	0.91	0.42	0.51	–		
Use of interdental brushes or dental floss (0 = no; 1 = yes)												
r	–0.18	–0.13	–0.20	–0.20	0.18	0.05	0.10	0.00	0.14	–0.12	1.00	
P value	0.01	0.06	<0.01	<0.01	0.01	0.43	0.14	0.95	0.05	0.08	–	
Dental check-up within last year (0 = no; 1 = yes)												
r	–0.18	–0.12	–0.14	–0.14	0.08	–0.08	0.16	–0.01	0.03	–0.01	0.22	1.00
P value	0.01	0.07	0.03	0.03	0.23	0.22	0.02	0.85	0.62	0.86	<0.01	–

– = no data.

Correlations among periodontal disease, serum lipids, and other relevant factors, such as gender, alcohol intake, number of teeth, BMI, use of interdental brushes or flossing, and having had a dental check-up within the last year, are shown in Table 2.

The percentage of sites with PD ≥4 mm had a significant negative association with TC, number of teeth, use of interdental brushes or flossing, and having had a dental check-up within the last year. The percentage of sites with CAL ≥4 mm had a

Table 3.

Relationship Between Serum Lipids and Periodontal Conditions

	Dependent Variables											
	Percentage of Sites With PD ≥4 mm				Percentage of Sites With CAL ≥4 mm				Percentage of Sites With BOP			
Independent Variable	Coeff.	*P* Value	95% CI	β	Coeff.	*P* Value	95% CI	β	Coeff.	*P* Value	95% CI	β
TC	−0.09	<0.01	−0.15 to −0.03	−0.19	−0.17	<0.01	−0.27 to −0.06	−0.20	−0.06	0.03	−0.12 to −0.01	−0.16
HDL-C					−0.02	0.82	−0.21 to 0.17	−0.01	−0.06	0.27	−0.15 to −0.09	−0.08
Gender (0 = male; 1 = female)					−10.47	<0.01	−16.79 to −4.16	−0.20				
Number of teeth	−0.46	<0.01	−0.67 to −0.26	−0.29	−1.54	<0.01	−1.89 to 1.20	−0.53				
Use of interdental brushes or dental floss (0 = no; 1 = yes)	−2.23	0.21	−5.72 to 1.25	−0.09	2.97	0.83	−5.23 to 6.48	0.01	−3.09	0.04	−6.08 to −0.09	−0.14
Dental check-up within last year (0 = no; 1 = yes)	−4.61	0.02	−8.32 to −0.90	−0.16	−6.52	0.04	−12.74 to −0.30	−0.13	−2.61	0.11	−5.80 to 0.58	−0.11
Constant	41.80	<0.01	28.31 to 55.29		114.60	<0.01	89.93 to 139.26		28.40	<0.01	17.42 to 39.38	
	R^2 = 0.16; *P* <0.01				R^2 = 0.06; *P* <0.01				R^2 = 0.09; *P* <0.01			

Coeff. = coefficient; CI = confidence interval.

significant negative association with TC, HDL-C, gender, number of teeth, use of interdental brushes or flossing, and having had a dental check-up within the last year. The percentage of sites with BOP had a significant negative association with TC, HDL-C, use of interdental brushes or flossing, and having had a dental check-up within the last year.

Results of the multiple regression analysis are shown in Table 3. The percentage of sites with PD ≥4 mm, CAL ≥4 mm, and BOP were used as dependent variables, and TC, HDL-C, LDL-C, gender, and the number of teeth, which showed a correlation with *P* <0.1 from the Pearson correlation analysis, were included in the model as independent variables. TC, number of teeth, and having had a dental check-up within the last year were significantly associated with the percentage of sites with PD ≥4 mm. TC, gender, number of teeth, and having had a dental check-up within the last year were associated with the percentage of sites with CAL ≥4 mm. TC and the use of interdental brushes or flossing were associated with the percentage of sites with BOP.

Table 4 shows the Pearson correlation coefficients used to estimate the relationship between serum lipids and inflammatory and nutritional factors. TC was shown to have a significant positive association with albumin, inorganic phosphorus, and calcium. HDL-C had a significant positive association with albumin and a negative association with CRP and IgG. LDL-C had a significant positive association with albumin, inorganic phosphorus, and calcium. Albumin was correlated with all serum lipids. However, IgG and γ-GPT were not correlated with any serum lipid.

The results of the multiple regression analysis between serum lipids and nutritional and inflammatory factors after controlling for confounding factors are shown in Table 5. Albumin, inorganic phosphorus, and calcium were associated with TC. Albumin and CRP were associated with HDL-C. Only inorganic phosphorus was associated with LDL-C.

DISCUSSION

This epidemiologic study revealed a negative association between periodontal disease and TC in

Table 4.

Pearson Correlation Coefficients and *P* Values Between Serum Lipids and Inflammatory and Nutritional Variables

Variable		TC	HDL-C	LDL-C	Albumin	Inorganic Phosphorus	Calcium	CRP	IgG	γ-GTP
TC	r	1.00								
	P value	–								
HDL-C	r	0.33	1.00							
	P value	<0.01	–							
LDL-C	r	0.83	−0.06	1.00						
	P value	<0.01	0.36	–						
Albumin	r	0.35	0.23	0.23	1.00					
	P value	<0.01	<0.01	<0.01	–					
Inorganic phosphorus	r	0.20	0.05	0.23	0.09	1.00				
	P value	0.01	0.44	<0.01	0.18	–				
Calcium	r	0.32	0.10	0.26	0.58	0.19	1.00			
	P value	<0.01	0.12	<0.01	<0.01	<0.01	–			
CRP	r	−0.14	−0.17	−0.02	−0.13	−0.06	0.06	1.00		
	P value	0.06	0.02	0.83	0.08	0.45	0.42	–		
IgG	r	−0.11	−0.13	−0.05	−0.10	−0.04	−0.03	0.12	1.00	
	P value	0.11	0.05	0.46	0.12	0.51	0.60	0.11	–	
γ-GTP	r	−0.02	−0.03	0.01	0.00	−0.05	0.04	−0.01	−0.02	1.00
	P value	0.75	0.63	0.93	0.98	0.45	0.59	0.91	0.72	–

– = no data.

Table 5.

Relationship Between Nutritional and Inflammatory Variables and Serum Lipids

	Dependent Variables											
	TC				HDL-C				LDL-C			
Independent Variable	Coeff.	*P* Value	95% CI	β	Coeff.	*P* Value	95% CI	β	Coeff.	*P* Value	95% CI	β
Albumin	27.04	<0.01	10.95 to 42.13	0.25	12.21	<0.01	4.26 to 20.15	0.22	0.22	0.15	−4.33 to 27.68	0.13
Inorganic phosphorus	8.11	0.03	0.95 to 14.46	0.14					8.63	0.02	1.68 to 15.58	0.18
Calcium	10.50	0.04	0.64 to 22.83	0.16					10.79	0.06	−0.52 to 22.10	0.17
CRP					−8.13	0.05	−16.11 to −0.16	−0.14	0.32	0.96	−12.76 to 13.40	0.00
Constant	−35.61	0.30	−124.53 to 38.50		9.95	0.56	−23.37 to 43.27		−63.19	0.13	−144.18 to 17.79	
	R^2 = 0.15; *P* <0.01				R^2 = 0.08; *P* <0.01				R^2 = 0.10; *P* <0.01			

Coeff. = coefficient; CI = confidence interval.

non-smoking elderly patients. There is the possibility of an inverse association between TC and periodontitis in the elderly. Our findings showed that TC levels were lower in patients with clinical periodontal disease. One possible explanation for the lower prevalence of periodontal disease among patients with elevated cholesterol is selective survival. Those who are susceptible to the biologic effects of high cholesterol levels tend to die before reaching an advanced age.[12,18] Furthermore, TC had a positive association with albumin in this study. Some reports[19-22] indicated that dietary intake influences serum albumin and TC. It is conceivable that subjects with high TC have a good nutritional status, and there is a possibility that higher TC improves the condition of the gingival tissue.

Although there was no significant correlation between serum lipids and periodontal disease in the present study, some studies[7,23-26] showed a significant relationship between periodontal disease and serum lipids. The previous studies did not restrict subject age and included smokers in the analysis. Therefore, our findings have a different basis from previous studies.

TC consists of HDL-C, LDL-C, and TGs. In our study, TGs were not included because non-fasting blood was measured. HDL-C functions to keep lipids (primarily triacylglycerol and cholesterol esters) in a soluble state as they are transported between tissues. The function of LDL-C is to carry triacylglycerols from the liver to the peripheral tissues where lipoprotein lipase degrades the lipids. Our results found that HDL-C had a significant association with albumin and CRP, but LDL-C had a significant association with albumin, calcium, and inorganic phosphorus. Albumin was associated positively with HDL-C and LDL-C because TC consists of HDL-C and LDL-C; i.e., HDL-C and LDL-C might have different mechanisms in periodontal disease.

HDL-C removes unesterified cholesterol from cell surfaces and other lipoproteins and esterifies it using phosphatidylcholine before delivering these cholesterol esters to the liver. This role and epidemiologic evidence that the concentration of HDL-C in plasma correlates inversely with the risk for coronary heart disease have earned it the reputation of being "good" cholesterol. Our study showed that higher HDL-C has a good influence on CRP. There is a potential explanation for this finding. Periodontal disease is a persistent bacterial infection that causes chronic inflammation in periodontal tissues.[27] HDL-C was observed to be anti-inflammatory in the absence of inflammation. However, after induction of an acute-phase response, HDL-C became proinflammatory.[28] This methanism is a local inflammatory process that mediates the destruction of periodontal tissues triggered by bacterial insult. HDL-C has an important role in inflammation, preventing it in the absence of acute inflammation or an acute-phase response.[27,29,30] According to Laurila et al.,[31] HDL-C concentrations and the ratios of HDL-C/TC were significantly decreased in subjects with chronic infection. The results of the present investigation are consistent with that study. Furthermore, it is well known that CRP is a positive marker of inflammation.[32] Chronic bacterial infections, such as periodontal disease, are one of the established risk factors for a moderately elevated CRP level.[32] There is a positive correlation between severity of periodontal disease and CRP level. Hence, it is reasonable that HDL-C has a negative relationship with CRP.

LDL-C is considered to be a precursor of vitamin D and provides unesterified cholesterol for cell surfaces. There is a possibility that aging decreases the production of vitamin D.[33] It is well known that there is a causal relationship between vitamin D and bone metabolism. Ergocalciferol (vitamin D_2), found in plants, and cholecalciferol (vitamin D_3), found in animal tissues, are sources of vitamin D. Vitamins D_2 and D_3 are not biologically active but are converted in vivo to the active form of the D vitamin by two sequential hydroxylation reactions. The first hydroxylation occurs at the 25-position and is catalyzed by a specific hydroxylase in the liver. The product of the reaction, 25-hydroxycholecalciferol (25-OH-D_3), is the predominant form of vitamin D in the plasma and the major storage form of the vitamin. 25-OH-D_3 is further hydroxylated at the 1-position by a specific 25-hydroxycholecalciferol 1-hydroxylase found primarily in the kidney, resulting in the formation of 1,25-diOH-D_3. The overall function of 1,25-diOH-D_3 is to maintain adequate plasma levels of calcium. The total amount of previtamin D_3 produced in the epidermis and dermis of young subjects is at least twice that of elderly subjects. There is a significant negative correlation of plasma 1,25-diOH-D_3 with age in subjects older than 60 years.[33] The effect of increased cholesterol, which includes increased LDL-C intake, may be enhanced by a significant increase in the intestinal absorption of vitamin D. High dietary intake of cholesterol might result in more minor periodontal disease in the elderly. The association of higher LDL-C with higher inorganic phosphorus and calcium might be partly attributable to bone metabolism. The effect of calcium on periodontal disease is likely related to alveolar bone change,[34,35] which eventually results in greater clinical attachment loss. There are reports[36-38] suggesting that oral bone mineral density correlates with skeletal bone density.

Finally, the limitations of the present study should be taken into consideration. Although a significant relationship between serum lipids and periodontal disease was observed, our study was cross-sectional.

Further longitudinal studies should be undertaken to confirm a causal relationship. TGs could not be measured because serum samples were not obtained from fasting subjects. Furthermore, data on serum parameters of mineral metabolism, such as vitamin D, were not available. It is possible that vitamin D contributes to improved bone metabolism.

CONCLUSIONS

Our results suggest that higher TC is associated with a lower prevalence of periodontal disease in nonsmoking elderly patients. There is a possibility that higher HDL-C has a good influence and prevents the persistent bacterial infection that causes chronic inflammation in periodontal tissues; higher LDL-C with higher inorganic phosphorus and calcium might be partly attributable to bone metabolism improvement. HDL-C and LDL-C might have different effects on the occurrence of periodontal disease.

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Original article

A longitudinal study of the relationship between diet intake and dental caries and periodontal disease in elderly Japanese subjects

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A longitudinal study of the relationship between diet intake and dental caries and periodontal disease in elderly Japanese subjects

Objective: We hypothesise that a difference in nutrition influences dental caries and periodontal disease. There are few previous studies especially longitudinal ones which have evaluated this hypothesis. This study investigated the relationship between nutritional intake, including milk and milk products (MMP), and dental disease, controlling for several confounding factors.

Material and methods: A group of 600 subjects aged 70, randomly selected for this study, included approximately the same number of male and female subjects. The number of teeth on which root caries had occurred or where there was a periodontal event over a 6-year period was measured. To determine quantitative food intake at baseline, a semi-quantitative food frequency questionnaire was used during face-to-face interviews by dieticians. The stepwise method of multiple linear regression analysis was used to identify independent predictors of the number of root caries or periodontal disease events during the 6 years. Intake of the six food groups includes (i) fish, shellfish, meat, beans and eggs; (ii) MMP; (iii) dark green and yellow vegetables (DYV); (iv) other vegetables and fruits; (v) cereals, nuts and seeds, sugar and sweeteners, confectioneries (CNSC) and (vi) fats and oils. The alcohol, gender and anthropometric evaluation including measurements of weight and height for the calculation of body mass index, educational level, the number of family members and the number of remaining teeth were used as independent variables.

Results: According to stepwise multiple regression analysis, two variables (quantity of MMP, and gender) were negatively associated with the number of root caries events during the 6 years. The standardised coefficients were −0.14 ($p = 0.035$) and −0.17 ($p = 0.007$) respectively. In addition, DYV were negatively, and three other variables (CNSC; alcohol; and the number of remaining teeth at baseline) were positively associated with the number of periodontal disease events during the 6 years. The standardised coefficients were −0.16 ($p = 0.001$), 0.11 ($p = 0.042$), 0.10 ($p = 0.041$) and 0.58 ($p < 0.001$) respectively.

Conclusion: Our results suggest that the intake of MMP in this elderly population correlated with root caries events. In addition, intake of vegetables negatively correlated, and intake of 'CNSC' positively correlated with periodontal disease events.

Keywords: milk intake, root caries, periodontal disease, elderly people.

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Introduction

Chewing food is important in the initiation of digestion. Food and nutrition are significant factors for humans at any age, but they are particularly important for the elderly. However, many elderly eat only soft, minced or even liquid foods because of their limited chewing ability due to tooth loss. As more teeth are lost because of periodontal disease and root caries as age increases[1,2], a strategy for preventing dental problems is necessary; this strategy should be helpful for all age groups. To

develop a preventive strategy, we need to determine the relationship between nutritional intake and dental disease.

A significant relationship between the number of present teeth and intake of vegetables and fruits, vitamins, minerals and dietary fibres has been shown, with subjects with dentures consuming fewer of these nutritious foods[3–6]. In addition, milk and milk products (MMP) seem to be associated with the prevention of dental caries and periodontal disease. Milk contains high levels of protein and calcium[7], and is often fortified with vitamins A and D; vitamin D enhancing calcium absorption[8]. *In vitro* experiments have demonstrated the potential of milk to remineralise carious enamel[9]. Therefore, we hypothesise that a difference in nutrition could influence dental caries and periodontal disease. There were few previous studies especially longitudinal ones which evaluated this hypothesis. This study evaluated the relationship between nutritional intake, including MMP, and dental disease, controlling for several confounding factors.

Materials and methods

Subjects

A longitudinal study was conducted in older adults residing in Niigata City, Japan. Initially, questionnaires were sent to all 4542 residents aged 70 years (born in 1927). From the responses, 600 people were randomly selected to have approximately the same number of each gender for the baseline survey. The number of subjects at baseline was 306 (51.0%) for males and 294 (49.0%) for females. All subjects were Japanese, in good general health, and did not require special care for their daily activities. Participants were asked to sign consent forms regarding the protocol using face-to-face interviews by the lead investigator, which was approved by the Ethics Committee of Niigata University School of Dentistry.

Dental examinations were carried out at baseline and once a year for 6 years (1998–2004); that is, seven times in 6 years. All the examinations, including dental examination and face-to-face food frequency questionnaire interviews, were conducted at eight local community centres in Niigata City.

Measurements

Root caries events. Four trained and experienced dentists assessed root caries. The examinations were conducted using mirrors and ball-pointed periodontal probes under artificial light, without bitewing radiographs. Root caries was diagnosed using the criteria of the World Health Organization[10]. First, it was determined whether a given surface was exposed or not. An exposed root surface was defined as at least 1 mm of visible root surface between the gingival crest and the cement-enamel junction or the restoration margin. All exposed root surfaces were examined and recorded. Root caries was defined as a lesion detected on an exposed root surface that felt soft or leathery to probing. For a single decay affecting both the crown and the root, the likely site of origin of the root was recorded as root caries.

Root caries incidence was tracked only on surfaces that were neither decayed nor filled at baseline examination. Whenever root caries was detected on a root surface that had previously been sound or non-exposed, it was counted as a disease event and these were counted each year. Surfaces where disease events occurred once were excluded from additional-year evaluations and finally, the number of surfaces on which a disease event occurred over the 6 years was converted into the number of teeth on which a disease event occurred in a given patient.

Inter-examiner reliability for surfaces was assessed for the four examiners using 18 volunteer patients in the University Hospital at the baseline year. A kappa score was calculated using five codes [sound, filled, decayed, filled (with decay) and bridge abutment: special crown or veneer/implant]. The kappa values between each pair of examiners were 0.84–0.97. During the survey, four examiners fulfilled the criteria using patients in the University Hospital.

Periodontal disease events. The periodontal examination included the assessment of attachment level at six sites around each tooth. Probing was performed using a pressure constant probe (Vivacare TPS Probe®, Schaan, Liechtenstein) and a probing force of 20 g. At first, the difference between attachment level at baseline and at follow-up for each site was calculated using site-level data. If the difference was ≥3 mm, it was counted as a periodontal disease event. Surfaces where disease events occurred once were excluded from additional-year assessments and data were rounded from site to tooth level. Finally, the number of teeth with an event per person was calculated.

The periodontal examination was carried out by four trained dentists under sufficient illumination using artificial light. Inter-examiner reliability for

attachment was assessed in the same way as for root caries and the percent agreement (± 1 mm) ranged from 70.0% to 100%, with the kappa (±1 mm) ranging from 0.62 to 1.00.

Nutritional measurements. To determine food intake, a semi-quantitative food frequency questionnaire was used during face-to-face interviews by the dieticians at baseline. The questionnaire contained six food groups and alcohol commonly consumed in Japan. For the dietary questionnaires, participants reported their average intake of a specified portion size for each food during the preceding month. For each food item on the questionnaire, four responses were possible, ranging from never to several times per day. Validity of the semi-quantitative food frequency questionnaire has been documented previously[11]. Responses to the individual food items were converted to an average daily intake of six groups of food for each participant including (i) fish, shellfish, meat, beans and eggs (FSMBE); (ii) MMP; (iii) dark green and yellow vegetables (DYV); (iv) other vegetables and fruits (OVF); (v) cereals, nuts and seeds, sugar and sweeteners, confectioneries (CNSC) and (vi) fats and oils (FO). In addition, the dieticians elicited what kinds of alcohol the subjects commonly consumed and the responses to these were converted to average daily intake. The alcohol included wine, beer and spirits such as whiskey, rum, gin, vodka. Inter-examiner reliability for the food frequency questionnaire interviews was not conducted.

Composition, blood measurements and characteristics. Anthropometric evaluation included measurements of weight and height for the calculation of body mass index (BMI). In addition, personal interviews were also conducted to obtain information regarding educational levels and the number of family members residing in the same household.

Statistical analysis

Of 600 participants, 261 persons (males: 144, females: 117) who had at least one tooth at baseline and participated in all annual investigations (seven occasions in total) were included in the analysis. Quantitative food intake and anthropometric markers were evaluated between males and females, with mean and standard deviations used to characterise continuous variables. In addition, after dividing subjects into two groups, subjects who drank milk every day (every day group) and subjects who did not (not every day group), the oral condition, BMI, educational level and the number of family members residing in the same household were compared. The amount of MMP was converted into milk intake per day according to the standard tables of food composition in Japan[12]. Finally, the stepwise method of multiple linear regression analysis was used to identify independent predictors of the number of root caries or periodontal disease events during the 6 years. Intake of the six food groups, alcohol, gender, BMI, educational level, the number of family members and the number of remaining teeth were used as independent variables. All calculations and statistical analyses including ANOVA were performed using the STATA™ software package (Stata Corp., College station, TX, USA).

Results

Table 1 shows characteristics of males and females at baseline. There were significant differences ($p < 0.001$) in food intake between genders except for OVF and FO. The intake of FSMBE, MMP and DYV was significantly higher ($p < 0.001$) in females than males and the intake of CNSC and alcohol was

Table 1 Demographic and eating habits among males and females at baseline[a].

	Males (n = 144)	*Females (n = 117)*	*p-value*
FSMBE (g/kg)	3.3 ± 1.1	3.8 ± 1.1	<0.001
MMP (g/kg)	3.1 ± 2.0	4.1 ± 2.4	<0.001
DYV (g/kg)	5.2 ± 1.6	6.5 ± 1.7	<0.001
OVF (g/kg)	0.9 ± 1.9	1.1 ± 2.2	0.516
CNSC (g/kg)	9.6 ± 3.9	9.2 ± 3.0	<0.001
FO (g/kg)	0.1 ± 0.2	0.1 ± 0.2	0.766
Alcohol (g/kg)	0.4 ± 0.4	0.1 ± 0.1	<0.001
Height (cm)	162.3 ± 5.4	148.6 ± 5.0	<0.001
Weight (kg)	58.5 ± 8.1	51.2 ± 7.8	<0.001
BMI (kg/m^2)	22.0 ± 2.6	22.8 ± 3.2	0.03
Number of remaining teeth	19.9 ± 7.8	18.6 ± 8.6	0.218
Education level (years)	10.7 ± 2.8	9.4 ± 2.0	<0.001
Number of family members	1.1 ± 0.3	1.3 ± 0.5	<0.001

[a]Mean ± 1 SD, using STATA statistical analyses.
BMI, body mass index; FSMBE, fish, shellfish, meat, beans and eggs; MMP, milk and milk products; DYV, dark green and yellow vegetables; OVF, other vegetables and fruits; CNSC, cereals, nuts and seeds, sugar and sweeteners, confectioneries; FO, fats and oils.

Table 2 The relationship between milk intake habits and each variable[a].

	Subjects who do not drink milk every day (n = 93)	*Subjects who drink milk every day (n = 168)*	*p-value*[b]
The amount of milk and the products per day (ml)[c]	57.0 ± 49.8	251.8 ± 110.5	<0.001
Number of the remaining teeth at baseline	17.9 ± 8.9	20.1 ± 7.7	0.023
Change in tooth loss during 6 years	2.0 ± 2.6	1.5 ± 2.0	0.122
Number of periodontal disease events	10.3 ± 7.3	9.6 ± 6.1	0.648
Number of root caris events[d]	1.6 ± 1.9	1.1 ± 1.6	0.024
Change in BMI during 6 years (kg/m^2)	0.4 ± 1.2	0.3 ± 1.5	0.505
Educational level (years)	10.1 ± 2.9	10.1 ± 2.3	0.757
Number of family members at baseline	1.2 ± 0.4	1.2 ± 0.4	0.492

BMI, body mass index.
[a]Mean ± 1 SD, using STATA statistical analyses.
[b]ANOVA adjusted by gender.
[c]We converted the amount of milk and milk products into milk intake per day according to the Standard Tables of Food Composition in Japan, Fifth Revised and Enlarged Edition.
[d]Root caries event was defined as the number of teeth on which a disease event occurred in a given patient during the follow-up period.

Table 3 Root caries and food intake: a 6-year assessment by stepwise multiple linear regression analysis[a].

	Dependent variable, the number of root caries events during 6 years					
Independent variables	*Coefficients*	*SE*	*p-value*	*95% confidence interval*		*β*
Milk and milk products (g/kg)	−0.10	0.05	0.035	−0.20	−0.07	−0.14
Gender	−0.58	0.21	0.007	−1.00	−0.16	−0.17
BMI (kg/m^2)	−0.05	0.04	0.137	−0.12	0.02	−0.09
Constant	3.62	0.86	0.001	<1.94	5.31	

BMI, body mass index.
[a]Independent variables included the six food groups [(1) fish, shellfish, meat, bean and eggs; (2) milk and its products; (3) dark green and yellow vegetables; (4) other vegetables and fruits; (5) cereals, nuts and seeds, sugar and sweeteners, confectionaries and (6) fats and oils]; alcohol; gender; BM at baseline; educational level; number of family members at baseline and the number of remaining teeth at baseline (n = 261, R^2 = 0.065, p = 0.0006).

significantly higher in males than females ($p < 0.001$).

As shown in Table 2, the amount of MMP per day was 251.8 ± 110.5 ml for the every day group and 57.0 ± 49.8 ml for the not every day group. The difference was significant by ANOVA adjusted by gender ($p < 0.001$). Furthermore, the number of remaining teeth was significantly higher in the 'every day' group compared with the 'not every day' group (20.1 ± 7.7 vs. 17.9 ± 8.9, respectively; p = 0.023) and root caries events during the 6 years were statistically higher in the 'not every day' group compared with the 'every day' group (1.6 ± 1.9 vs. 1.1 ± 1.6, respectively; p = 0.024). Root caries developed over the 6-year study in the subjects who did not drink milk every day and who did, these being 61.3% and 48.2% respectively (data not shown in a table). The odds ratio of root caries occurrence for the subjects who did not drink milk every day was 1.69 (p = 0.043). In addition, periodontal disease progression developed over the course of the study in this latter group of subjects compared with those who drank every day, these being 95.7% and 95.8% respectively (data not shown in a table). The odds ratio of periodontal disease progression for the subjects who did not drink milk every day was 0.97 (p = 0.959).

Regarding root caries the stepwise multiple regression results show that two variables (amount of MMP and gender) were negatively associated with the number of root caries events during 6 years (Table 3). The standardised coefficients (β)

Table 4 Peridontal disease and food intake: a 6-year assessment by stepwise multiple linear regression analysis[a].

	Dependent variable, the number of periodontal disease events during 6 years					
Independent variables	*Coefficients*	*SE*	*p-value*	*95% confidence interval*		*β*
Dark green and yellow vegetables (g/kg)	−0.64	0.19	0.001	−1.00	−0.27	−0.16
Cereals, nuts and seeds, sugar and sweeteners, confectionaries (g/kg)	0.19	0.09	0.042	0.01	0.38	0.11
Alcohol (g/kg)	1.87	0.91	0.041	0.08	3.66	0.10
Number of remaining teeth at baseline	0.47	0.04	<0.001	0.39	0.55	0.58
Constant	2.13	1.59	0.182	−1.00	5.27	

BMI, body mass index.
[a]Independent variables included the six food groups [(1) fish, shellfish, meat, bean, eggs; (2) milk and its products; (3) dark green and yellow vegetables; (4) other vegetables and fruits; (5) cereals, nuts and seeds, sugar and sweeteners, confectionaries and (6) fats and oils]; alcohol; gender; BMI at baseline; educational level; number of family members at baseline and number of remaining teeth at baseline (n = 261, R^2 = 0.382, $p < 0.001$).

were −0.14 (p = 0.035) and −0.17 (p = 0.007) respectively. As for periodontal disease, the results of stepwise multiple regression analysis are shown in Table 4. DYV was negatively, and three other variables (CNSC; alcohol and the number of remaining teeth at baseline) were positively associated with the number of periodontal disease events during the study. The standardised coefficients (β) were −0.16 (p = 0.001), 0.11 (p = 0.042), 0.10 (p = 0.041) and 0.58 ($p < 0.001$) respectively.

Discussion

In this study, there was a significantly negative relationship between the amount of daily milk intake and the number of root caries. The number of root caries events during the 6 years was significantly lower among subjects with a greater intake of MMP. These findings indicate that MMP may help to reduce root caries in the elderly.

The elderly population experiences more gingival recession and more root caries than the younger generation[13,14] and this has been shown to be associated with tooth loss[15]. Milk appears to have many physical properties of a good saliva substitute. For example milk contains calcium, vitamin D, riboflavin, B complex vitamins, vitamin A and phosphorus[16]. Gedalia *et al.*[9] demonstrated that human enamel that had softened with an acidic beverage could be rehardened with milk or saliva exposure. Remineralisation could be a significant factor in determining milk's anticariogenic properties and in particular, casein phosphopeptide substantially increases the level of calcium phosphate in dental plaque, maintaining a state of supersaturation with respect to tooth enamel by decreasing demineralisation and enhancing remineralisation[17]. Reduction in demineralisation by calcium and phosphate may result from lowering the critical pH of the plaque because of diffusion of calcium and phosphate into the plaque. Postulated mechanisms of this diffusion include buffering, salivary stimulation and reduction of bacterial adhesion[18]. For example, microbiological parameters such as *Streptococcus sobrinus* or *Actinomyces viscosus* in the oral cavity have been shown to be negatively correlated with milk casein[19–21]. In addition, several components of milk, including inorganic and organic phosphates and the amino acid residues, have been shown to buffer pH levels[22].

The odds ratio of root caries occurrence for subjects who did not drink milk was 1.69 (p = 0.043). This finding shows that these subjects have the 1.69-fold higher risk for root caries occurrence. The relationship was weak, even if it was statistically significant.

According to these findings, it is probable that the intake of MMP is related to the reduction of root caries in the elderly. It was thought that remineralisation might be milk's most important anticariogenic factor. However, previous findings are based on *in vitro* research. To our knowledge, this study is the first study to examine the relationship between the intake of MMP and the incidence of root caries in a large elderly population. Further prospective studies are needed to determine the actual nature of this relationship.

In terms of other foods, the number of periodontal disease events during the 6 years significantly decreased with increasing amount of intake of DYV. In addition, periodontal disease events

significantly increased with increasing intake of CNSC.

In a previous report, we showed a significantly positive relationship between nutrient intake, such as minerals and vitamins from food, especially from vegetables, and tooth loss[6]. Many surveys have been performed regarding the relationship between vitamin C and periodontal disease. National Health and Nutrition Examination Surveys (NHANES) III, which included 39 695 subjects, showed a significantly positive relationship between low vitamin C intake and periodontal disease. Even after controlling for age, gender, smoking and gingival bleeding, the level of periodontitis in subjects with a low dietary intake of vitamin C was 1.19 times greater than that of subjects with a higher intake of vitamin C[23]. The World Health Organization also showed similar findings[24]. It is likely that vegetable intake is related to the incidence of periodontal disease in the elderly. However, OVF had no significant impact on the study population concerning periodontal disease in this study. A significant relationship has been difficult to establish, as the results have been easily confounded by other factors such as supplements intake. In the present study, about 40% of subjects took vitamins or mineral supplements. However, it was impossible to evaluate the nutritional intake including supplements because of lack of detailed information about the supplements. Further studies should be undertaken to confirm the observations in this study.

Cereals, nuts and seeds, sugar and sweeteners, confectioneries were related positively to dental plaque formation[25]. Furthermore, some reports show that alcohol intake might influence the severity of periodontal disease[26–28]. In our study, periodontal disease events significantly increased with increasing alcohol intake.

However, there are some limitations to our study. A semi-quantitative food frequency questionnaire was used to determine quantitative food intake, but some researchers suggest that nutritional epidemiology such as the 24-h dietary recall and food intake records may not provide a complete picture of what is being eaten on a routine basis. Other methods, such as food frequency questionnaires, are criticised because people, and particularly the elderly, may not recall exactly what they have eaten over a period of time. Among the various methods, precise weighing methods are said to measure nutrients most accurately. In addition, we could not confirm a clear cause–effect relationship between nutrition and dental caries and periodontal disease because of a lack of longitudinal change in nutrition during 6 years. To explore the actual relationship, further prospective studies and clinical trials will be necessary.

In conclusion, our results suggest that the intake of MMP in this elderly population correlated with root caries events. In addition, the intake of vegetables negatively correlated, and the intake of 'CNSC' positively correlated with periodontal disease events. Nutrition and diet contribute to oral craniofacial development and to the maintenance of tissues throughout life. The findings of our study suggest that elderly people should consume adequate daily amounts of milk and vegetable, and limit the intake of CNSC to reduce dental caries and/or periodontal disease events.

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