Cohort Study of the Total Leukocyte Count and Periodontal Disease Among Company Employees

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Abstract

There have been few epidemiological studies of the relationship between the leukocyte count and dental disease. In the present study, therefore, we investigated the relationship between oral health indicated by the Community Periodontal Index of Treatment Needs (CPITN) and the total leukocyte count in the cohort study. The 1,035 subjects were male factory workers employed at a chemical factory in Osaka, Japan. Their oral conditions were recorded as the CPITN score. The relationship between the total leukocyte count and the oral condition of the subjects classified according to their smoking habits was investigated over a 5-year period. Among the current smokers, the total leukocyte count was highest each year for the group with CPITN level 4, followed by those with CPITN levels 3 and 2 in descending order, showing that the total leukocyte count was reduced as the periodontal diseases ameliorated. Among the nonsmokers, the total leukocyte count was high every year in the group with CPITN levels 4 or 3 compared to that of the group with CPITN level 2. The fluctuations of the total leukocyte count in current smokers and nonsmokers whose CPITN score increase or decreased in five years was investigated. There were no significant differences among the all groups.

Key words: periodontal disease, total leukocyte count, CPITN, Japanese company employees

Introduction

Eighty-four percent of adults were found to have evidence of the gum diseases gingivitis and periodontitis, and 54.2% of the elderly have severe periodontal disease in Japan.¹⁾ Due to the high occurrence of dental disease, the potential association with Ischemic Heart Disease (IHD) may have implications for millions of people.

A matched case-control study of 200 participants in Finland showed significant positive associations between myocardial infarction (MI) and composite dental indices combining caries, periodontitis, periapical lesions, pericoronitis, and edentulousness.²⁾ In another study of 88 men, Mattila et al. reported a positive dose-response association between coronary atherosclerosis and the composite dental index.³⁾ The composite dental index was also linked to ischemic events in patients with

IHD at entry.⁴⁾

In a cohort study of people initially free of IHD, the relative risk for IHD of 1.25 (95% CI, 1.06 to 1.48) for individuals with periodontal disease and 1.23 (95% CI, 1.05-1.44) for those with complete tooth loss were reported, compared with people with no dental disease.⁵⁾

Recent reports about the relationships between other chronic infections and IHD or inflammatory mediators and IHD also support a role of chronic dental infection in IHD.^{6,7)} Loesche postulates that oral diseases result in chronic infections in the host that leads to low-level bacteremia and an elevated leukocyte count. In addition, he speculated that periodontal disease results in the exposure of the host to an endotoxin that affects endothelial integrity, the metabolism of plasma lipoproteins, blood coagulation, and the function of platelets.⁸⁾ An elevated leukocyte count may, of course, also be a marker for chronic inflammation from causes other than smoking habits. Although leukocytes are traditionally thought of as defenders against infections, they also play an important role in microvascular perfusion. It has been reported that the probability of the development of IHD increases in individuals with a high leukocyte count (even when the count is still within the normal range).⁹⁻¹²⁾

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A number of prospective epidemiologic studies have shown that the leukocyte count is a good predictor of IHD.⁹⁻¹²⁾ Yoshida et al.¹³⁾ investigated the relationship between total leukocyte count and periodontal disease as classified by the Community Periodontal Index of Treatment Needs (CPITN) in 1,241 male Japanese factory workers. It appeared that there was a significant relationship between total leukocyte count and the symptom of periodontal disease. Kweider et al.¹⁴⁾ showed that blood taken from periodontal disease patients had significantly higher total leukocyte counts and fibrinogen levels than blood taken from 50 similarly aged control patients who did not have periodontal disease.

These are cross-sectional studies, showing the results estimated from surveys at certain time points. In this report, we present the results of a cohort study of the relationship between leukocyte count and periodontal diseases among the employees of a large organization over a period of 5 years.

Methods

Study population and survey method

A sample constituted by only men was selected from a defined worksite, a chemical plant in Osaka, Japan. The experimental design is summarized in Fig. 1.

Initially 1,431 Japanese factory workers at the chemical plant were examined, and 1,035 who met the following health conditions were selected as participants in the study.

1. Males aged 20-59 years.
2. Those who were not under medical treatment.
3. Those who did not have atherosclerosis, cardiovascular disease or diabetes.
4. Those whose total leukocyte count was measured once every year during the 5-year study period.
5. Those whose oral condition was measured in both 1992 and 1996.

Recruitment Phase Survey Methods

The study was conducted by a team of investigators with common training at the Osaka Prefectural College of Health Science, Habikino, Japan. The study had a common core protocol, and the same laboratory was used for all hematological tests.

The subjects were invited to attend a morning clinic. A standard medical and smoking history was obtained, and height, weight, blood pressure, and oral conditions were measured. A blood sample was taken with minimal venous stasis.

The categories of tobacco use were defined as follows: Current smokers were subjects who had a habit of smoking any number of cigarettes at the time when the interview was

Fig. 1 Experimental design

Table 1 Distribution of CPITN score of current smokers and nonsmokers in initial and final assessment

Current smokers					Nonsmokers				
Group	CPITN score		n	Total	Group	CPITN score		n	Total
	Initial year (1992)	Final year (1996)				Initial year (1992)	Final year (1996)		
C-CPITN4 group	4	4	19	19(45.5 ± 7.6yr.)	N-CPITN4 group	4	4	5	5(51.4 ± 7.1yr.)
C-CPITN3 group	3	3	121	121(39.0 ± 8.9yr.)	N-CPITN3 group	3	3	55	55(43.5 ± 10.0yr.)
C-CPITN2 group	2	2	140	140(30.3 ± 8.2yr.)	N-CPITN2 group	2	2	125	125(34.6 ± 10.1yr.)
C-CPITN1 group	1	1	1	1(40yr.)	N-CPITN1 group	1	1	2	2(38yr.)
C-CPITN0 group	0	0	0	0	N-CPITN0 group	0	0	0	0
C-group I	0	1	0			0	1	0	
	0	2	13			0	2	9	
	0	3	7			0	3	7	
	0	4	0			0	4	0	
	1	2	44	215(34.5 ± 9.5yr.)	N-group I	1	2	32	168(36.7 ± 10.4yr.)
	1	3	16			1	3	15	
	1	4	2			1	4	3	
	2	3	87			2	3	68	
	2	4	11			2	4	10	
	3	4	35			3	4	24	
C-group II	4	3	26			4	3	8	
	4	2	4			4	2	5	
	4	1	0			4	1	0	
	4	0	0			4	0	0	
	3	2	81	114(37.5 ± 10.1yr.)	N-group II	3	2	50	70(38.7 ± 10.5yr.)
	3	1	0			3	1	0	
	3	0	1			3	0	0	
	2	1	0			2	1	4	
	2	0	2			2	0	2	
	1	0	0			1	0	1	

CPITN: Community Periodontal Index of Treatment Needs (): Mean age of group n: Number of subjects

conducted. Nonsmokers were those subjects who did not currently smoke. There were 610 current smokers (58.9 %) and 425 nonsmokers (41.1 %).

Laboratory Methods

For the measurement of total leukocyte count, each blood sample was immediately inserted into a specimen tube containing EDTA. The total leukocyte count was measured by an automated cell counter (Coulter-made S-plus; Coulter Electronics, Hialeah, FL, USA).

At least 5% of the samples sent to the laboratory were unidentifiable split-sample duplicates. The coefficients of variation for these blind duplicates were 2% for total leukocyte counts.

Measurement of Oral Conditions

The oral condition parameters recorded were caries status (decayed, missing, and filled teeth) and periodontal status (Community Periodontal Index of Treatment Needs, CPITN).¹⁹⁾ The periodontal probe used was a Periodontal Examination Probe recommended by the World Health Organization (Morita Co., Osaka, Japan).

All subjects were examined by three experienced dental hygienists. The three examiners underwent a two-day training session shortly before the data collection. The examination was performed with the use of a lighted mouth mirror. Third molars were excluded from all assessments.

Statistical Methods

The statistical analyses were conducted using the SPSS 6.1 J computer software program. Within the groups of current smokers and nonsmokers, differences in the total leukocyte count and oral conditions were analyzed by unpaired t-test. Significance was defined as $p < 0.05$.

Results

Table 1 shows the distribution of the CPITN scores at the initial (1992) and final (1996) assessments, in the current smokers and nonsmokers. The percentage of individuals with an unchanged CPITN score at the initial and final surveys was 45.2% among the current smokers and 46.0% among

Table 2 Variation of the total leukocyte count in the current smokers and nonsmokers CPITN score since the initial survey

Year	Total Leukocyte count (cells/ μ l)			
	C-group I Mean $\pm$ SE (n=215)	C-group II Mean $\pm$ SE (n=114)	N-group I Mean $\pm$ SE (n=168)	N-group II Mean $\pm$ SE (n=70)
1992	7187 $\pm$ 126	7117 $\pm$ 166	6200 $\pm$ 112	6150 $\pm$ 133
1993	6852 $\pm$ 124	6796 $\pm$ 173	6029 $\pm$ 106	6110 $\pm$ 193
1994	6821 $\pm$ 112	6898 $\pm$ 173	5895 $\pm$ 118	5774 $\pm$ 140
1995	6861 $\pm$ 125	6723 $\pm$ 171	5751 $\pm$ 110	5934 $\pm$ 139
1996	7091 $\pm$ 117	7052 $\pm$ 176	5961 $\pm$ 119	5956 $\pm$ 162
1997	7187 $\pm$ 126	7117 $\pm$ 166	6200 $\pm$ 112	6150 $\pm$ 133

n: Number of subjects

nonsmokers. The percentage of those with a CPITN score that was decreased since the initial survey (i.e., their oral conditions improved) was 37.0% among the current smokers and 35.3% among the nonsmokers. Increases in the CPITN score (exacerbation of periodontal disease) in the same period were noted in 17.8% of the current smokers and 18.7% of the nonsmokers.

Figures 2 and 3 show the sequential changes in the total leukocyte count of the subjects exhibiting a constant CPITN level between the initial and final surveys (classified according to the CPITN levels and smoking habits). Among the current smokers, the total leukocyte count was highest each year for the group with the highest possible CPITN score, followed by those with the CPITN levels 3 and CPITN 2 in descending order, showing that the total leukocyte count was reduced as the periodontal diseases improved (the leukocyte count for the group with the CPITN level of 0 or 1 was omitted in the comparison because there were only a few individuals in these groups). Among the nonsmokers, the total leukocyte count was high in each year in the groups with the CPITN level 4 or 3 compared to that of the group with the CPITN level 2 (the data for the groups with the CPITN level of 0 or 1 were omitted for the reason given above). These data demonstrate that the total leukocyte count was lowest in each year in the groups in which the periodontal diseases were mildest.

Table 2 shows the fluctuations of the total leukocyte count in the current smokers and nonsmokers whose CPITN score increased or decreased since the initial survey. There were no significant variations in all groups.

Fig. 2 Serial changes in the total leukocyte count of the current smokers with constant CPITN scores (1992 to 1996)
The data are mean $\pm$ S.E.

Fig. 3 Serial changes in the total leukocyte count of the nonsmokers with constant CPITN scores (1992 to 1996)
The data are mean $\pm$ S.E.

Discussion

The association between total leukocyte count and IHD is almost entirely independent of the other main cardiovascular risk factors.¹²⁾ When Sweetnam et al.¹⁶⁾ excluded the 1,122 men who had any evidence of pre-existing disease, the age-adjusted mean difference in total leukocyte count between the men who developed IHD and those who did not increased to 0.88×10^9 /liter.

The mechanism by which leukocytes may promote atherosclerosis and thrombosis is thought to include pressure-dependent plugging of microvessels and rheologic properties such as reduced deformability.¹⁸⁾

A periodontal disease is defined as an inflammation that is caused by bacteria in dental plaque. Although limited to the oral cavity, this process is responsible for a sustained inflammatory condition that starts with gingivitis in youth and continues to tooth loss in aging. This disease is liable to be a factor contributing to a high total leukocyte count over an extended period. Cross-sectional study by Yoshida et al.¹³⁾ investigated the relationship between dental disease and total leukocyte counts in Japanese factory workers; there was a significant correlation between their total leukocyte counts and the CPITN scores, and it was found that the subjects with severe cases of periodontal disease exhibited significantly high total leukocyte counts. Kweider et al.¹⁴⁾ studied 50 consecutive patients aged 25 to 50 with periodontal disease and 50 age-matched controls who had relatively healthy periodontal conditions as measured by the

gingival and CPITN scores and no evidence of disease that may produce elevated fibrinogen or total leukocyte counts. Bivariate analyses indicated that the periodontal disease patients had higher mean scores for the plaque index, gingival index, CPITN, fibrinogen and total leukocyte counts. The above observations suggest that inflammatory dental disease may be a determinant of fibrinogen and total leukocyte counts in the general population.

Here, we conducted a cohort study of employees of a large company to investigate the correlation between the severity of periodontal diseases and the total leukocyte count. It was found that the total leukocyte count was significantly higher in the subjects affected by more severe periodontal disease in comparison with those unaffected or only slightly affected by the same disease. It was also found that the exacerbation of periodontal disease is associated with significant increases in the total leukocyte count among smokers. Our study thus substantiated the results of a controlled study by Kweider et al.¹⁴⁾ and a cross-sectional study by Yoshida et al.¹³⁾ on the relationship between periodontal diseases and total leukocyte count.

Smoking causes risk factors for periodontal disease. It also contributes to risk factors for cardiovascular disease. Preliminary epidemiologic studies have suggested that there is an association between edentulousness and cardiovascular disease, and between periodontal disease and cardiovascular disease¹⁸⁾. It could be speculated that these associations are coincidental, reflecting a lifestyle of personal neglect, which predisposes a person to both heart disease and dental disease.

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