치의학석사 학위논문

Association between periodontitis and dyslipidemia based on the fourth Korea National Health and Nutrition Examination Survey

제4기 국민건강영양조사를 이용한 한국인의 치주질환과 이상지질혈증의 상관성

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치의학과

이 준 범

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지도교수 배 광 학

이 논문을 치의학석사 학위논문으로 제출함

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이 준 범

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위 원 장 _____ (인)

부 위 원 장 _____ (인)

위 원 _____ (인)

Abstract

Association between periodontitis and dyslipidemia based on the fourth Korea National Health and Nutrition Examination Survey

Lee,JunBeom

Department of Dentistry

School of Dentistry

Seoul National University

Aims: The aim of this study was to examine whether dyslipidemia is associated with periodontitis in a representative sample of

Korean adults who were involved in the Fourth Korea National Health and Nutrition Examination Survey (KNHANES).

Materials and methods: A total of 18,210 subjects over 19 years of age who participated in KNHANES were examined. Dyslipidemia is defined according to the definition proposed by the Korean Society of Lipidology and Atherosclerosis. The periodontal status of the patients was assessed by the Community Periodontal Index (CPI). Multivariate logistic regression analysis was carried out and adjusted for sociodemographics, oral health behaviors and status, and general health behavior. All analyses considered a complex sampling design, and multivariate analysis was also performed in the subgroups (age, gender, and current smoking status).

Results: Multivariate logistic regression analysis revealed significant associations between dyslipidemia except pre-hypercholesterolemia and periodontitis. In the subgroup analysis,

periodontitis was significantly associated with hypo-HDL-cholesterolemia and had a potential association with hyper-TG in subjects younger than 40 years. The adjusted ORs were greater in the present smoker group than the non-smoker group.

Conclusions: Dyslipidemia except pre-hypercholesterolemia is associated with periodontitis.

Clinical Relevance

Scientific rationale for the study: Although an association between periodontitis and dyslipidemia has been reported in some studies, more studies are needed to confirm the association. In particular, few studies have examined the relationship between dyslipidemia and periodontitis based on a comprehensive, nationwide, and representative survey in Asia.

Principle findings: Among a representative sample of adults of Korean nationality, this study found that periodontitis is associated with dyslipidemia.

Practical implications: Periodontitis is associated with dyslipidemia in Koreans under the age of 40 years, and further studies are needed to determine if there is a cause and effect relationship between these two conditions.

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Keywords : periodontal disease, dyslipidemia, relationship, Korea National Health and Nutrition Examination (KNHANES)

목차

표목차

Introduction

Cardiovascular disease (CVD) is the main cause of morbidity and mortality in the world, and atherosclerosis is a major component of CVD (Mehra et al. 2007). Abnormal serum lipid level is important in the development of atherosclerosis because atheromatous plaque can be initiated by the focal accumulation of lipids (Ross et al. 1999). Dyslipidemia (DLP) is a disorder of serum lipid level that includes elevated total cholesterol (TC), elevated triglycerides (TG), elevated low density lipoprotein cholesterol (LDL-C), and decreased high density lipoprotein cholesterol (HDL-C). Many studies reported that DLP is a major risk factor for CVD (Kashyap 1997).

Periodontitis is a chronic inflammatory disease (Li et al. 2009) that leads to the destruction of the connective tissue and bone anchoring the teeth to the jaws (Williams 1990). Periodontitis is one of the most common chronic diseases in the world (Albandar

et al. 1999). The prevalence of periodontitis is 30.7% among Korean adults (Korea Center for Disease Control and Prevention & Ministry of Health and Welfare 2008). There are several studies on the association between periodontitis and systemic alterations including diabetes, rheumatoid arthritis, and osteoporosis (Genco 1996).

Many studies have suggested a potential association between periodontitis and DLP (Cutler et al. 1999, Fentoğlu et al. 2009, Taleghani et al. 2010), but the mechanism remains controversial. Although DLP has become common in Korea (Lee et al. 2012), few studies have examined the relationship between DLP and periodontitis based on a comprehensive, nationwide, and representative survey in Korea.

The aim of this study was to examine whether DLP is independently associated with periodontitis using a representative sample of Korean adults adjusted for socio-demographics, oral

and general health behaviors, and oral health status.

Materials and Methods

Study design and subject selection

The data included a subset of the Fourth KNHANES conducted from 2007 to 2009 by the Korea Center for Disease Control and Prevention (KCDC). The sampling protocol for KNHANES was designed to involve a complex, stratified, multistage, probability-cluster survey of a representative sample of the non-institutionalized civilian population in South Korea. The survey was performed by the Korean Ministry of Health. The target population of the survey was all non-institutionalized civilian Korean individuals one year of age or older. The survey employed stratified multistage probability sampling units based on the geographic area, gender, and age, which were determined based

on the household registries of the 2005 National Census Registry, the most recent five-year national census in Korea. Using the 2005 census data, 200 primary sampling units (PSU) were selected annually across Korea. The final sample set for KNHANES included 13,800 households. A total of 18,210 subjects 19 years of age and older participated in KNHANES, but only 15,534 of the subjects, who participated in both the periodontal examination and DLP measurement, were analyzed in this study. A detailed description of the sampling was described in the KNHANES report (KCDC 2009).

Clinical variables

Dyslipidemia

DLP was defined according to the criteria of the Korean Society of Lipidology and Atherosclerosis: TC level is normal when ≤ 200

mg/dL, pre-hyper-TC when 200-239mg/dL, and hyper-TC when ≥240mg/dL. TG level is normal when ≤ 200 mg/dL and hyper-TG when >200mg/dL. HDL-C level is normal when >40mg/dL and hypo-HDL-C when ≤40mg/dL. LDL-C level is normal when <130 mg/dL, pre-hyper-LDL when 130-159mg/dL, and hyper-LDL when ≥160mg/dL. This definition is not different from the National Cholesterol Education Program Adult Treatment Panel III (NCEP ATP III and modified NCEP ATP III).

The fourth KNHANES survey did not measure LDL-C level. Therefore, this study focused on the association of TC, TG, and HDL levels with periodontitis.

Periodontitis

The WHO community periodontal index (CPI) was used to assess periodontitis. Periodontitis is defined as a CPI greater than or equal to 'code 3,' which indicates that at least one site had a >

3.5 mm (code 4 > 5.5 mm) pocket. The index tooth numbers were 11, 16, 17, 26, 27, 31, 36, 37, 46, and 47 according to the Federation Dentaire Internationale (FDI) system.

A CPI probe that met the WHO guidelines was used (WHO 1997). The mouth was divided into sextants. An approximately 20 g probing force was used. In the 2007 to 2009 KNHANES, 13 in 2007, 24 in 2008 and 29 in 2009 trained dentists examined the periodontal status of the subjects. In the calibration training, the number of study subjects was 20 in 2007, 15 in 2008, and 30 in 2009. Periodontitis was defined as a CPI greater than or equal to 'code 3', which indicates that at least one site had a > 3.5 mm (code 4 > 5.5 mm) - pocket. The inter-examiner means of the Kappa value were 0.72 (0.69 to 0.77) in 2007 (KCDC 2008), 0.89 (0.55 to 1.00) in 2008 (KCDC 2009), and 0.75 (0.53 to 0.94) in 2009 (KCDC 2010).

Covariates

The socio-demographic variables included gender, age, household income, and educational level. Household income was the family income adjusting for the number of family members. It was measured all around the age and the household income was categorized into 4 quartiles from top to bottom. The educational level was assessed by the most advanced diploma. The oral health behaviors included the use of dental floss. For general health behaviors, alcohol consumption experience in the lifetime of the patients and current smoking status were included. According to the current smoking status, the subjects were divided into three groups (non-smokers: those who had never smoked or had smoked fewer than 100 cigarettes in their life, current smokers: those who were currently smoking and had smoked 100 cigarettes or more in their whole life, past smokers: those who had smoked in the past but were no presently smoking). The oral and general

health status included the number of active caries teeth, presence of diabetes mellitus (DM), and obesity. The number of teeth with active caries was defined as the number of teeth which had any active carious lesions. The presence of diabetes mellitus (DM) was determined in self-administration questionnaires as follows: "Have you ever been diagnosed with diabetes mellitus by doctor? Yes or no?" Obesity was classified into three groups based on the BMI value according to the guidelines from the Korean Society for the Study of Obesity (KSSO) and the World Health Organization (WHO) criteria: 1) underweight (< 18.5 kg/m^2); 2) normal weight (18.5 to 24.9 kg/m^2); and 3) obese (≥25 kg/m^2).

Socio-demographic variables, health behaviors, and oral health behaviors were examined using a self-administration questionnaire survey.

Statistical analysis

The individual weighted factors were used, and the complex sampling design of the survey was considered to obtain the variances. Multivariate logistic regression analyses were applied to examine the relationships between DLP and periodontitis. The odds ratios of periodontitis for DLP were adjusted for the above-mentioned covariates in the logistic model. Since the interaction terms of periodontitis with age, gender, and smoking was significant, subgroup analyses were performed to obtain estimates stratified according to the effect modifiers. We adopted 40 years of age as the cut off since the prevalence of periodontitis generally increases rapidly after that age. Each effect modifier was excluded from its multivariate model of the subgroup except age. Statistical analyses were performed using SPSS version 20.0 software.

Results

Periodontitis defined as a CPI code ≥ 3 was 35.8%. Tables 1, 2, and 3 list the characteristics of the study subjects categorized by periodontal status. The demographics of the target population were as follows: the mean age was 44.90 years (44.43 to 45.37), and the percentage of males was 49.5% (48.8 to 50.2).

Table 4 showed the associations between DLP and periodontitis in the multivariate logistic regression models. Hyper-TC, hyper-TG, and hypo-HDL-C exhibited higher odds ratios (ORs) for periodontitis, but pre-hyper-TC was not significantly associated with periodontitis. The adjusted ORs were 1.04 (95% CI: 0.94 to 1.16) for pre-hyper-TC, 1.17 (95% CI: 0.99 to 1.37) for hyper-TC, 1.18 (95% CI: 1.04 to 1.33) for hyper-TG, and 1.16 (95% CI: 1.03 to 1.31) for hypo-HDL-C. The results of the subgroup analyses were also presented in Table 4. Pre-hyper-TC was not associated with periodontitis in

any strata. In the group less than 40 years of age, only hypo-HDL-C was significantly associated with periodontitis and hyper-TG might be significant. However, in the group aged 40 years or more, it was not associated with periodontitis. For gender, hyper-TC and hyper-TG were significantly associated with periodontitis in the male groups, while hypo-HDL-C showed the association in the female groups. For smoking status, hyper-TG and hypo-LDL-C were significantly associated with periodontitis in current smokers, but no associations were observed in non-smokers.

Discussion

In this study, an association was found between DLP and periodontitis after adjusting for socio-demographic variables, oral and general health behavior, and oral health status. The results showed that periodontitis was significantly associated with only hypo-HDL-C in subjects less than 40 years of age, and the

association was higher in smokers. Interestingly, subjects 40 years of age or older were not significantly associated with DLP, although periodontitis and DLP are more prevalent in older subjects. These results also showed that a gender difference exists in association between periodontitis and DLP components. Hyper-TC and hyper-TG was significant in males, while hypo-HDL-C was significant in females. Further studies are necessary to elucidate the age and gender difference.

Ebersole et al. (1999) demonstrated significant increases in the serum lipid profile (TC, TG, LDL, and HDL) in periodontal disease. Theirs was the first study on the relationship between serum lipid level and periodontitis, but it was performed on non-human primates. Although several cross-sectional studies reported a positive association between serum lipids level and periodontitis, the results are somewhat controversial. Some articles stated that there is a relationship between TC level and

periodontitis (Katz et al. 2001, 2002), while others showed a relationship between TG level and periodontitis (Cutler et al. 1999). In addition, it was shown that a relationship exists between periodontitis and both TC and TG levels (Lösche et al. 2000). There was also a cohort study on the association between chronic periodontitis and serum lipid level that showed that patients with chronic periodontal disease had higher values only for serum TG level (Taleghani et al. 2010).

A few studies on the association between DLP and periodontitis were completed in several Asian countries using a non-representative sample. Moeintaghavi et al. (2005) revealed a positive relationship between TC and TG levels and periodontitis in Iran. The historical cohort study of Taleghani et al. (2010) reported that only TC level was significantly higher in the group of patients with chronic periodontitis. The results of these studies

are similar to ours in that there was a significant association between DLP and periodontitis.

A possible role of DLP on periodontitis is known to cause hyperactivity of leukocytes (Croft et al. 1990, Krause S et al. 1993). Progressive periodontitis in adults was demonstrated to be frequently associated with an increased concentration of oxygen radicals (Krause S et al. 1990). Some reports stated that there is a bi-directional relationship between DLP and periodontitis (Fentoglu et al. 2008). The possible mechanisms explaining the association between periodontitis and DLP include: infection (Lopes-Virella 1993, Samra et al. 1996), bacterial lipopolysaccharides and serum lipoproteins (Akerlund et al. 1986, Feingold et al. 1987, Reidy et al. 1978), lipoprotein-associated inflammatory proteins (Chait et al. 2005), and effects of dietary lipids on immune system functions (Chapkin et al. 1990).

Our study had several limitations. The periodontal status was assessed by the CPI. Although CPI is an easier way of evaluating the periodontal treatment needs in a community setting, it can overestimate or underestimate the prevalence of periodontitis because the use of representative teeth includes pseudo pockets (Kingman & Albandar 2002). Also, there is no statistical research about hyper-LDL-C - another component of DLP. Some reports showed an association between hyper-LDL-C and periodontitis (Katz et al. 2002, Fentoğlu et al. 2009). In addition, this study couldn't consider other potential confounders such as sedentary life styles and fatty food consumption as they were not examined in this survey. In the further studies, they should be included as confounders. One of the most important limitations of the present study is its cross-sectional design, which makes it impossible to determine the cause and effect relationship between DLP and periodontitis.

Nevertheless, an association was found between DLP and periodontitis after adjusting for various potential confounders including socio-demographic variables, oral and general health behavioral factors, and oral health status. Most studies did not consider as many confounders as the present study. The confounding factors were not restricted to the present general health and socioeconomic status, but also the oral and general health behaviors that could affect the periodontal health and DLP. In addition, this study was carried out comprehensively on a Korean representative population sample.

Conclusion

Periodontitis is significantly associated with DLP except pre-hyper-TC as defined using the Korean Society of Lipidology and Atherosclerosis criteria. More prospective cohort studies are required to allow for a better understanding of the underlying

biological mechanisms exhibiting a cause-effect relationship between DLP and periodontitis.

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The authors declare no conflicts of interest related to this study

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Table 1. Univariate comparisons of the socio-demographic characteristics in subjects with and without periodontitis

	Total	No periodontitis		Periodontitis	
	n	n	%* (95% CI)	n	%* (95% CI)
Age (n=16067)	44.20	40.43 (39.91-40.95)†		51.86 (51.28-52.44)†	
Gender (n=16067)					
Male	6837	3877	61.5 (59.6-63.3)	2960	38.5 (36.7-40.4)
Female	9230	6438	72.6 (71.0-74.1)	2792	27.4 (25.9-29.0)
Highest diploma (n=15997)					
Primary school	4366	2206	48.6 (46.0-51.1)	2160	51.4 (48.9-54.0)
Middle school	1828	994	54.0 (50.8-57.0)	834	46.0 (43.0-49.2)
High school	5536	3853	72.3 (70.5-74.0)	1683	27.7 (26.0-29.5)
≥ University or College	4267	3219	76.2 (74.3-78.0)	1048	23.8 (22.0-25.7)
Household income‡ (n=15684)					
< 25 %	3127	1693	56.7 (53.8-59.4)	1434	43.3 (40.6-46.2)
25 - 50 %	3934	2415	64.6 (62.4-66.8)	1519	35.4 (33.2-37.6)
50 - 75 %	4266	2846	68.4 (66.3-70.4)	1420	31.6 (29.6-33.7)
> 75 %	4357	3126	72.9 (70.7-75.0)	1231	27.1 (25.0-29.3)

*Weighted percent and 95% confidence interval

†Weighted mean and 95% confidence interval

‡Household income: monthly average family equivalent income (=monthly average household income/$\sqrt{\text{(the number of household members)}}$

Table 2. Univariate comparisons between the subjects with and without periodontitis in oral and general health status

	No periodontitis		Periodontitis	
	n	%* (95% CI)	N	%* (95% CI)
Active caries (n=16067)	0.84 (0.79−0.89)†		0.97 (0.91−1.04)†	
Total cholesterol (n=15534)				
Normal	6919	69.9 (68.3−71.4)	3487	30.1 (28.6−31.7)
Pre−hyper−TC	2369	62.0 (59.7−64.2)	1570	38.0 (35.8−40.3)
Hyper−TC	688	57.8 (54.1−61.4)	501	42.2 (38.6−45.9)
Triglyceride (n=15534)				
Normal	8635	69.1 (67.6−70.5)	4455	30.9 (29.5−32.4)
Hyper−TG	1341	56.6 (53.6−59.4)	1103	43.4 (40.6−46.4)
HDL−cholesterol (n=15534)				
Normal	7884	69.6 (68.1−71.0)	3944	30.4 (29.0−31.9)
Hypo−HDL−C	2092	59.3 (56.7−61.8)	1614	40.7 (38.2−43.3)
DM (n=16042)				
No	9770	68.5 (67.0−69.9)	5103	31.5 (30.1−33.0)
Yes	530	44.4 (40.8−48.0)	639	55.6 (52.0−59.2)

Obesity (n=15911)				
Normal	6624	68.7 (67.1−70.3)	3461	31.3 (29.7−32.9)
Underweight	525	78.2 (74.5−81.5)	179	21.8 (18.5−25.5)
Obese	3045	61.7 (59.5−63.8)	2077	38.3 (36.2−40.5)

*Weighted percent and 95% confidence interval

†Weighted mean and 95% confidence interval

Table 3. Univariate comparisons of the oral and general health behaviors in subjects with and without periodontitis

	No periodontitis		Periodontitis	
	n	%* (95% CI)	n	%* (95% CI)
Oral health behaviors				
Use of floss (n=16033)				
No	8763	65.1 (63.5−66.7)	5334	34.9 (33.3−36.5)
Yes	1531	80.2 (78.0−82.3)	405	19.8 (17.7−22.0)
General health behaviors				
Alcohol consumption experience in a lifetime (n=16005)				
No	1365	61.1 (58.0−64.0)	922	38.9 (36.0−42.0)
Yes	8916	67.8 (66.3−69.3)	4802	32.2 (30.7−33.7)
Present smoking status (n=15993)				
Past smoker	1517	57.5 (55.1−59.9)	1285	42.5 (40.1−44.9)
Current smoker	1997	61.0 (58.8−63.2)	1499	39.0 (36.8−41.2)
Non−smoker	6760	73.1 (71.5−74.6)	2935	26.9 (25.4−28.5)

*Weighted percent and 95% confidence interval

Table 4. Adjusted odds ratios (OR) and 95% confidence intervals (CI) of periodontitis (CPI ≥ 3) for MS and its components in total and for each subgroup

	Total	Age group		Gender		Current smoker	
		Age (<40)	Else (≥40)	Male	Female	Yes	No
Pre-hyper-TC	1.04 (0.94-1.16)	0.86 (0.68-1.08)	1.04 (0.93-1.18)	1.10 (0.95-1.27)	1.00 (0.87-1.16)	1.14 (0.94-1.38)	1.01 (0.90-1.14)
Hyper-TC	1.17 (0.99-1.37)	1.20 (0.80-1.81)	1.10 (0.93-1.29)	1.46 (1.14-1.89)	1.01 (0.82-1.20)	1.36 (0.97-1.91)	1.12 (0.94-1.35)
Hyper-TG	1.18 (1.04-1.33)	1.27 (0.98-1.66)	1.06 (0.92-1.21)	1.21 (1.03-1.41)	1.16 (0.97-1.39)	1.32 (1.07-1.63)	1.12 (0.97-1.30)
Hypo-HDL-C	1.16 (1.03-1.31)	1.36 (1.08-1.73)	1.10 (0.96-1.26)	1.11 (0.96-1.29)	1.25 (1.07-1.48)	1.21 (1.00-1.47)	1.12 (0.97-1.30)

The multivariate logistic regression model was adjusted for socio-demographic variables (age, gender, family income, educational level), oral health behaviors (use of floss), general health behaviors (alcohol consumption experience in a lifetime, present smoking status), oral health status (active caries) and general health status (diabetes mellitus and obesity).
In the subgroup, each effect modifier was excluded from its multivariate model except age.

국문초록

제4기 국민건강영양조사를 이용한 한국인의 치주질환과 이상지질혈증의 상관성

이준범
서울대학교 치의학대학원
치의학과

목적: 본 논문의 목적은 제 4 기 국민건강영양조사를 이용하여 한국인의 치주질환과 이상지질혈증 간의 상관성에 대해 알아보는 것이다.

연구 및 방법: 제 4 기 국민건강영양조사에 참여한 20 세 이상의 남녀 성인은 18,210 명이었다. 이상지질혈증은 한국지질동맥경화학회에서 제시한 기준에 따라 정의하였고, 치주질환은 WHO 에서 제시한 Community Periodontal Index 를 따라 평가하였다. 교란변수를 사회인류학적 요인, 구강건강과 전신 건강 상태 및 구강건강과 전신건강 행태로 나누어 다변량 로지스틱 회귀분석을 하였다. 모든

분석은 복합표본을 고려하여 시행하였고 나이, 성별, 현재 흡연여부에 대한 집단별 통계분석도 시행하였다.

결과: 다변량 로지스틱 회귀분석 결과 pre-hypercholesterolemia 를 제외한 이상지질혈증과 치주질환 사이에 유의한 상관성을 보였다. 집단별 분석 결과 40 세 미만의 집단에서 치주질환은 hypo-HDL-cholesterolemia 와 유의한 상관관계를 보였고 hyper-TG 와는 상관성을 보였다. 또한 현재 흡연을 하는 집단이 비흡연자 집단보다 오즈비가 컸다.

결론: 다변량 로지스틱 회귀분석 결과 pre-hypercholesterolemia 를 제외한 이상지질혈증과 치주질환 사이에 유의한 상관성을 보였다.

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주요어: 치주질환, 이상지질혈증, 상관관계, 국민건강영양조사 (KNHANES)