In addition, there were significant relationship between occlusal condition (dental status) and physical fitness, especially and one-leg standing time with eyes open after controlling for confounding factors. One-leg standing time with eyes open is an index of equilibrium. Several investigators reported the influences of oral status on motor performance and muscle strength of the lower extremities [20, 21]. Some relation between occlusion and posture regulation has been reported [22-24]. Abnormal habits such as a one-sided mastication may be precipitated by a change of occlusal support. Subsequently, abnormal habits may lead to a disequilibrium of systemic muscle balance and may influence systemic equilibrium function.

One limitation of our study is that we could not confirm a clear cause-effect relationship among ACE, occlusal conditions, and physical fitness in the elderly because of our cross-sectional design. To explore the actual relationship, further prospective studies and clinical trials will be necessary.

In conclusion, this study suggests that there was a significant relationship between ACE genotype and physical performance. In particular, the subjects with the ACE DD genotype were noted to have low muscle strength.

Acknowledgments

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Table 1. Comparison of selected characteristics between the males and females.

Variable		Males (n=228)	Females (n=203)	*p* value
		Mean±SD (n)	Mean±SD (n)	
Angiotensin converting enzyme gene I/D polymorphism				
	DD	(26)	(27)	
	ID	(85)	(84)	
	II	(88)	(64)	0.319
Nuber of present teeth		16.3±9.9 (226)	15.7±9.5 (195)	0.498
Eichner index				
	A	(55)	(41)	
	B	(103)	(92)	
	C	(68)	(62)	0.719
Hand-grip strength (kg)		36.2±5.7 (215)	23.8±4.2 (176)	<0.001
Leg extension strength (kg)		35.8±10.3 (188)	24.6±7.5 (144)	<0.001
Stepping (time/10 sec)		83.7±15.6 (197)	75.7±13.3 (158)	<0.001
One-leg standing time with eyes open (sec)		54.8±43.2 (199)	35.3±36.3 (166)	<0.001
10-m walking speed (sec/10m)		4.6±1.2 (195)	5.2±1.0 (160)	<0.001
BMI (%)		22.4±2.8 (219)	23.3±3.3 (191)	0.004
Total cholesterol (mg/dL)		187.3±28.9 (218)	206.9±30.0 (187)	<0.001
Total protein (g/dL)		6.9±0.5 (218)	7.0±0.5 (187)	0.205
IgA (mg/dL)		284.1±129.4 (218)	246.1±86.9 (187)	0.001
IgG (mg/dL)		1284.7± 264.6 (218)	1310.5±285.8 (187)	0.346

Table 2. Relationship between angiotensin converting enzyme gene I/D polymorphism and physical fitness

		Hand-grip strength (kg)		Leg extension strength (kg)		Stepping (time/10 sec)		One-leg standing time with eyes open (1:120 sec/0:<120)		10-m walking speed (sec/10 m)	
Independent variables		Beta	*p* value	Beta	*p* value	Beta	*p* value	Beta	*p* value	Beta	*p* value
Angiotensin converting enzyme gene I/D polymorphism	DD (reference, Beta=0)	0.00	-	0.00	-	0.00	-	0.00	-	0.00	-
	ID	0.09	0.019	0.09	0.135	0.13	0.041	0.08	0.200	-0.11	0.088
	II	0.12	0.003	0.09	0.146	0.03	0.643	0.08	0.188	-0.15	0.023
BMI (%)		0.09	0.004	0.21	<0.001	-0.03	0.557	-0.16	0.001	0.06	0.283
Gender (male=0, female=1)		-0.79	<0.001	-0.55	<0.001	-0.26	<0.001	-0.14	0.005	0.23	<0.001
Constant		-	<0.001	-	<0.001	-	<0.001	-	<0.001	-	<0.001
n		389		331		354		410		354	
R^2		0.62		0.32		0.09		0.06		0.08	

Table 3. Relationship between angiotensin converting enzyme gene I/D polymorphism and physical fitness after adjustment for confounding factors using multiple regression analysis

		Hand-grip strength (kg)		Leg extension strength (kg)		Stepping (time/10 sec)		One-leg standing time with eyes open (1:120 sec/0:<120)		10-m walking speed (sec/10m)	
Independent variables		Beta	*p* value	Beta	*p* value	Beta	*p* value	Beta	*p* value	Beta	*p* value
Total cholesterol (mg/dL)		-0.05	0.148	0.01	0.912	0.03	0.596	0.05	0.422	-0.08	0.205
Total protein (g/dL)		0.01	0.776	0.04	0.581	-0.03	0.695	-0.02	0.809	-0.04	0.547
IgA (mg/dL)		-0.05	0.126	0.00	0.922	0.07	0.221	0.03	0.553	0.03	0.634
IgG (mg/dL)		-0.04	0.354	-0.10	0.100	-0.03	0.648	-0.03	0.670	0.07	0.318
Dental status (Eichner Index Class C=1, no=0)		0.01	0.687	0.02	0.669	-0.04	0.458	-0.11	0.028	0.09	0.073
Angiotensin converting enzyme gene I/D polymorphism	DD (reference, Beta=0)	0.00	-	0.00	-	0.00	-	0.00	-	0.00	-
	ID	0.09	0.022	0.09	0.143	0.13	0.042	0.07	0.250	-0.11	0.093
	II	0.12	0.004	0.08	0.177	0.03	0.610	0.08	0.209	-0.14	0.039
BMI (%)		0.10	0.001	0.22	<0.001	-0.03	0.622	-0.15	0.002	0.04	0.419
Gender (male=0, female=1)		-0.78	<0.001	-0.55	<0.001	-0.26	<0.001	-0.13	0.014	0.25	<0.001
Constant		-	<0.001	-	0.042	-	<0.001	-	0.037	-	<0.001
n		382		325		347		403		347	
R^2		0.63		0.33		0.09		0.07		0.10	

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B. 指定課題名 ： 平成19年度医療技術評価総合研究事業
「地域住民の口腔保健と全身的な健康状態の関係についての総合研究」

C. 研究協力課題 ：
「高齢者における歯周病と血清脂質の関係について」

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E. 研究目的：

口腔健康と全身健康の関係、とりわけ歯の喪失の予防という観点についてこれまで多くの疫学調査が実施されてきた。しかしながら高齢者における歯周疾患と栄養学的関係においては不明な点が多く、高齢者の歯の喪失には歯周病が大きな要因となっていることから、高齢者における歯周病予防対策は必要不可欠である。

従来より血清脂質は高齢者における重要な死亡因子のひとつとされており、歯周疾患との関連性が注目されている。

本研究の目的は非喫煙高齢者における歯周疾患と血清脂質の関係を評価することである。

F. 研究方法 ：

厚生科学研究（高齢者の口腔健康状態と全身健康状態の関係についての総合研究）において、平成10年度に行われたベースライン調査で対象とした70歳の高齢者599名のうち、8年後のフォローアップ調査に参加し、血清資質を測定した非喫煙者の有歯顎者（男性63名、女性171名）を本研究対象とした。

歯周組織診査は智歯を含むすべての機能歯を対象に一歯あたり6点について歯周ポケット、アタッチメントレベル、BOPを測定した。血清脂質は総コレステロール、HDLコレステロール、LDLコレステロールを測定し、他にカルシウム、無機リン、アルブミン、CRP、Ig.Gについて生化学検査を実施した。

G. 研究結果および考察

重回帰分析の結果、4mm以上のポケットの部位と4mm以上のアタッチメントレベルの部位、BOPはトータルコレステロールと負の相関が見られた。トータルコレステロールの標準化係数は上記の因子に対し、-0.17（p＝0.009）、-0.16（p=0.001）、-0.21（p=0.001）である。ピアソンの相関係数によるとトータルコレステロールはアルブミン（r=0.32、p=<0.001）、無機リン（r=0.18、p=0.007）、カルシウム（r=0.26、p=<0.001）と有意に関連があった。

HDL コレステロールはアルブミン（r=0.20、p=0.0002）、CRP（r=-0.20、p=0.006）と有意に関連があった。LDL コレステロールはアルブミン（r=0.20、p=0.002）、無機リン（r=0.23、p=0.001）、カルシウム（r=0.22、p=0.001）と関連があった。

これらの所見から健常老人においては栄養状態がよく、生体維持に必須であるコレステロールの摂取も多いことから、相対的に高コレステロールであることが歯周病の進行抑制につながると考えられる。

H. 結論 ：

本研究の結果より、従来の知見とは異なり、老人において高い血清コレステロール値は歯周疾患の進行を抑制する働きがあるかもしれない。また、HDL と LDL においては歯周疾患に働きかける機能に差がみられる可能性がある。

I. 研究発表論文：

なし

A. 宛名：分担研究者　宮崎秀夫　殿

B. 指定課題名：地域住民の口腔保健と全身的な健康状態の関係についての総合研究

C. 研究協力課題：日本人高齢者における歯周病と血清中レジスチン、アディポネクチン濃度との関連

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E. 研究目的：歯周病は糖尿病の前段階とも言えるメタボリックシンドロームや肥満との関連が指摘されている。本研究の目的は、脂肪細胞から産生されるレジスチン、アディポネクチン、IL-6およびTNF-αの血清中濃度と歯周病との関連を明らかにすることである。

F. 対象および方法

2004 年に新潟で実施された高齢者調査（78 歳、n=418）における歯周組織検査の結果から、10歯以上を有し ≥6 mmの歯周ポケットを有する歯周病群(n=84)と、比較的歯周組織の状態のよいコントロール群(n=74)を選択し、血清中のレジスチン、アディポネクチン、IL-6、TNF-αの濃度を測定し比較した（モデル１、n=158）。さらにプロービング時の出血（BOP）を考慮し、歯周病群から BOP ≤ 10%の者を除き、コントロール群からは BOP > 10%の者を除いたモデル２(n=107)において同様の分析を行った。歯周組織と各種アディポカインの関連性については、性別、喫煙、BMI、血糖値で調整した多変量ロジスティック回帰分析および共分散分析（ANCOVA)を行った。

G. 研究結果および考察

モデル１では、歯周病群においてレジスチンが高く、アディポネクチンが低い傾向にあったが、有意ではなかった。モデル２では歯周病群でレジスチンが有意に高かった（p=0.024）。高レジスチン（≥5.3ng/mL)を従属変数とした多変量ロジスティック回帰分析において、歯周病群では高レジスチンと有意な関連性が認められた（モデル１: OR 2.0; 95%CI, 1.2-4.0）。更に BOP を考慮したモデル２では、より強い関連性を認めた(OR 2.9; 95%CI, 1.2-6.9)。 ANCOVA では、BOP10%を超える歯周病群において調整後の平均レジスチンレベルが有意に高く(6.11±3.54ng/mL vs. 4.78±2.95ng/mL, p=0.037)、アディポネクチンは歯周病群において低い傾向にあったが有意ではなかった。

H. 研究発表論文　Journal of Periodontal Research (in press)

The relationship between periodontal condition and serum levels of resistin and adiponectin in elderly Japanese

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Running title: Serum resistin and adiponectin levels in periodontitis

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Key words: resistin, adiponectin, elderly, periodontitis

Abstract

Background and Objective: Diabetes and periodontitis are associated with each other. Adipokines, specifically adiponectin and resistin, are secreted from adipocytes and are thought to cause insulin resistance in rodents. Additionally, adiponectin and resistin may play a role in inflammation and immune responses. The aim of this study was to clarify the relationship between serum levels of adipokines and periodontal conditions in elderly Japanese people with and without periodontitis.

Material and Methods: A total of 158 Japanese men and women (78 years old) with or without periodontitis were selected for the study. Serum adiponectin, resistin, IL-6, and TNF-α concentrations were compared between subjects with and without periodontitis.

Results: Serum resistin levels and total leukocyte counts in subjects with periodontitis were higher than in control subjects. No significant differences were observed in adiponectin, IL-6, and TNF-α levels between subjects with and without periodontitis. Logistic regression analysis showed that periodontitis with at least one tooth that displayed a probing pocket depth of ≥6 mm was significantly associated with higher

serum resistin levels (odds ratio [OR], 2.0; 95%CI, 1.0-4.0). When excluding periodontitis subjects with ≤10% of bleeding on probing (BOP) and excluding control subjects with >10% BOP, differences between groups and OR increased. Serum adiponectin tended to decrease in patients with periodontitis, albeit not significantly.

Conclusion: Increased serum resistin levels were significantly associated with periodontal condition, especially when considering BOP, in elderly Japanese people. There was also a trend, though non-significant, toward decreased levels of adiponectin in subjects with periodontitis.

Introduction

The local host response to periodontopathogens and their products includes the proliferation and release of macrophages and cytokines. These immune components are thought to play a crucial role in periodontitis. Various cytokines, including interleukin-1β (IL-1β) and tumor necrosis factor-α (TNF-α), are determinants of the progression of periodontitis (1). Additionally, increased circulating interleukin-6 (IL-6)

levels appear to be correlated with disease severity (2).

Recent evidence indicates that periodontitis may have profound effects on systemic health. Several studies have evaluated the relationship between diabetes, metabolic syndrome, and periodontal disease (3-6). Most epidemiological evidence indicates that individuals with diabetes tend to have a more rapid progression of periodontitis than non-diabetics (7).

Adipose tissue produces and releases a variety of inflammatory factors, including adiponectin, resistin, leptin, and visfatin, as well as cytokines such as TNF-α, IL-6, and monocyte chemoattractant protein -1 (MCP-1). These factors and cytokines influence insulin resistance and are thought to play a role in inflammation and immune responses (8). Resistin received its name from the original observation that it induced insulin resistance in mice. Additionally, resistin is down-regulated in mature murine adipocytes cultured in the presence of insulin-sensitizing drugs, including thiozolidinediones (9). Recent studies in humans suggest that very little resistin is expressed in adipocytes; resistin is largely expressed in monocytes, macrophages (10), and bone marrow (11),

which are all linked to immune response (8).

In contrast, adiponectin levels are decreased in individuals with obesity, type2 diabetes, and cardiovascular disease (12). In addition, adiponectin influences a wide range of inflammatory pathologies, such as rheumatoid arthritis (13). Furthermore, adiponectin inhibits osteoclast formation stimulated by lipopolysaccharide (LPS) from *Actinobacillus actinomycetemcomitans* (14). Regulation of adiponectin is provided by inflammatory cytokines such as IL-6 (15) and TNF-α (16). Inflammatory endotoxins induce resistin in human macrophages via a cascade involving the secretion of inflammatory cytokines such as IL-6 and TNF-α (17). Although altered adipokine levels have been observed in a variety of systemic inflammatory conditions, only a few studies reported that the association between periodontitis and adipokines such as leptin and adiponectin. Leptin levels in gingival crevicular fluid decreased as the periodontal disease progressed (18). Although Iwamoto et al. demonstrated that periodontal treatment did not influence circulating adiponectin level (19), a relationship between periodontal conditions and resistin levels has not been examined. Bleeding frequency,

which is a direct indicator of gingival inflammation, is considered to be a strong risk factor for periodontal disease progression in elderly people (20). Here we investigated the relationship between periodontal conditions and adiponectin, resistin, IL-6, and TNF-α in a community of elderly people.

Material and methods

Subjects

In 1998, total 4542 people who were at 70 years old and resided in Niigata, Japan, were sent a written request to participate in the survey and were informed of the purpose of this survey. After two requests, 81.4% (3695) responded positively to participate in the survey. After considering the availability of resources, 600 subjects were randomly selected. The participants signed informed consent forms that described the protocol and were approved by the Ethics Committee of Niigata University Graduate School of Medical Dental Sciences. The methods used in this study have been described in detail