Research Article

Serum Ratio of Leptin to Adiponectin in Patients with Chronic Periodontitis and Type 2 Diabetes Mellitus

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Background. Serum ratio of leptin to adiponectin has been reported to be a useful index of insulin resistance. Since these two adipokines could also be involved in many immunoinflammatory reactions, this ratio might be associated with some inflammatory diseases such as periodontitis. The present study aims to explore the difference in serum ratio of leptin/adiponectin among patients with diabetes and periodontitis, patients with periodontitis only, and healthy people and find out the correlation between this ratio and periodontal parameters. **Method.** 15 patients with chronic periodontitis and type 2 diabetes, 15 patients with chronic periodontitis only, and 15 healthy controls were selected. Clinical indexes and periodontal parameters were recorded and serum leptin and adiponectin levels were tested by ELISA kits. **Result.** The ratio of leptin/adiponectin is significantly different among three groups; the T2 DM + CP group has the highest ratio (1.91 ± 0.48) and the healthy group has the lowest ratio (0.65 ± 0.13). What is more, the ratio of leptin/adiponectin has strong positive correlation with periodontal parameters ($P < 0.001$). **Conclusions.** Chronic periodontitis could influence the level of adipokines in serum and change the ratio of leptin/adiponectin, and the effect would be enhanced combining with type 2 diabetes.

1. Introduction

Type 2 diabetes mellitus is a chronic metabolic disease because of insulin resistance, while obesity may be a very important factor associated with insulin resistance and type 2 diabetes mellitus [1]. Researches during the last 20 years showed that the adipose tissue, in addition to being a specialized organ for fat storage and release, should also be considered an active endocrine gland capable of synthesizing and secreting adipokines such as adiponectin and leptin [2]. These adipokines could not only affect the insulin sensitivity, but also be involved in many immunoinflammatory reactions [3].

Chronic periodontitis is an infective disease damaging the periodontal tissue, and the local host response to periodontal pathogens and their products is thought to play a crucial role during this process. Studies recently found that periodontitis might be related to several systemic diseases especially diabetes mellitus [4–6]. Chronic periodontitis and type 2 diabetes could influence themselves bidirectionally because

of some common immunoinflammatory mechanisms and some common risk factors such as obesity [7]. Thus, Saito suggested that obesity, type 2 diabetes, and chronic periodontitis are closely associated, exhibiting a triangular relationship [8], and the adipokines might play an important role in this association.

Leptin and adiponectin are two adipocytokines that have been shown to be associated with insulin resistance [9, 10]. Leptin is a 16-kDa nonglycosylated peptide hormone. It is synthesized mainly in adipocytes and can regulate weight control and modulate other pathophysiological functions such as insulin sensitivity and inflammation [11]. Adiponectin is a 244-residue protein that is produced mainly by white adipose tissue (WAT). Adiponectin increases fatty acid oxidation and reduces the synthesis of glucose in the liver and has been reported to have anti-inflammatory properties [12].

Several studies recently have reported associations between the ratio of leptin/adiponectin and insulin resistance [13–16]. An increased leptin/adiponectin ratio has been

shown related to insulin resistance in obesity, type 2 diabetes mellitus, or metabolic syndrome.

Since leptin and adiponectin are also involved in the inflammatory process, this biomarker might play some roles in prediction of chronic inflammations. However, the association of leptin/adiponectin ratio in patients with chronic periodontitis and type 2 diabetes mellitus remains unknown. We supposed that the ratio of leptin/adiponectin was different between patients with diabetes mellitus and periodontitis and patients with periodontitis only. Thus, the present study evaluated the difference in serum ratio of leptin/adiponectin among these patients.

2. Materials and Methods

2.1. Participant Selection. 30 patients were selected from the clinic of Department of Stomatology, Peking University Third Hospital, Beijing, China, from March 2011 to August 2012. 15 patients were with type 2 diabetes and chronic periodontitis (T2 DM + CP), but without any complications of diabetes; 15 patients were with chronic periodontitis (CP), but systemically healthy. The criteria of chronic periodontitis were signs of clinical inflammation, more than two sites in different quarters with probing depth (PD) ≥ 5 mm and attachment loss (AL) ≥ 2 mm, and radiographic evidence of bone loss. Patients with type 2 diabetes were diagnosed by Endocrinology Department of Peking University Third Hospital; the criteria of type 2 diabetes were according to the diagnostic criteria from WHO in 1999. 15 healthy subjects were selected from the staff of the hospital, who showed a clinically healthy periodontium, PD ≤ 3 mm, AL = 0, with no evidence of bone loss on radiographs, and no systemic disease.

The exclusion criteria included: (1) aggressive periodontitis, (2) hypertension, (3) smoking habit, (4) heart diseases, (5) pregnancy, (6) any other systemic disease that can alter the course of periodontal disease, (7) those who had any course of medication affecting periodontal status within 1 month, and (8) those who had received periodontal therapy within 6 months. Informed consent was signed by each volunteer at the beginning of this investigation while the ethical clearance was approved by the Ethical Committee of Peking University.

2.2. Blood Collection. 5 mL of fasting venous blood was collected from each participant using nonanticoagulated blood tube. After 1-hour clotting at room temperature, serum was separated from blood by centrifuging at 3500 rpm ($r = 8$ mm) for 15 minutes at 4°C. Then, the serum was immediately transferred to several Eppendorf tubes and stored at -70°C until the time of assay.

2.3. Leptin and Adiponectin Analysis. The leptin and adiponectin levels were assayed using enzyme linked immunosorbent assay (ELISA) Kit (R&D, USA) according to the instructions of the manufacturer. Serum samples were diluted 1:100 for adiponectin analyses and 1:10 for leptin analyses. The minimum detection limits were 0.1 ng/mL for adiponectin and 7.8 pg/mL for leptin. All samples were duplicated.

2.4. Statistical Analyses. ANOVA one-way variance analysis was performed for comparing the levels of leptin, adiponectin, and ratio of leptin/adiponectin among three groups. The Spearman rank correlation coefficient test was used to investigate the relationship between leptin, adiponectin, or leptin/adiponectin ratio and clinical parameters. All tests were done by SPSS software, and P values < 0.05 were considered statistically significant.

3. Results

The clinical and periodontal parameters of three groups are displayed in Table 1. The T2 DM + CP group consists of 7 males and 8 females, and the mean age is 43.33 ± 10.08 ; the CP group consists of 8 males and 7 females, and the mean age is 43.87 ± 7.30 ; the healthy group consists of 7 males and 8 females, and the mean age is 37.53 ± 6.37 . There is no significant difference in the age and gender distribution among three groups. The T2DM + CP group and CP group has similar BMI index while the healthy group is lower. The T2DM + CP group has higher HbA1c and higher fasting blood glucose (FBG) than CP group and healthy group. Additionally, there is no significant difference in periodontal parameters including PD, AL, and bleeding index (BI) between T2 DM + CP group and CP group, but these parameters are much lower in healthy group.

The serum concentration of leptin, adiponectin, and the ratio of leptin/adiponectin are shown in Table 2. The level of leptin in serum is highest in T2 DM + CP group and lowest in healthy group, while the level of adiponectin is similar between T2 DM + CP group and CP group but much higher in healthy group. The ratio of leptin/adiponectin is significantly different among three groups; the T2 DM + CP group has the highest ratio and the healthy group has the lowest ratio.

Spearman rank correlation coefficient test between serum level of leptin, adiponectin, and ratio of leptin/adiponectin and PD, AL, and BI in all observations was shown in Table 3. The concentration of serum leptin had significant positive correlation with periodontal parameters while the concentration of serum adiponectin had significant negative correlation with periodontal parameters. The ratio of leptin/adiponectin in this study showed strong positive correlation with periodontal parameters ($P < 0.001$).

4. Discussion

The present study demonstrated significant difference in leptin, adiponectin, and ratio of leptin/adiponectin among T2 DM + CP group, CP group, and healthy group.

The relationship between periodontitis and type 2 diabetes mellitus has been discussed widely in the past several decades. Many studies showed that diabetes is an independent risk factor of chronic periodontitis [17] and periodontitis has been thought to be the sixth complication of diabetes [18], while, on the other hand, periodontitis could worsen the metabolism of diabetes [19]. Although the detail of this bidirectionally association is not clear yet, the cytokines may play an important role during the process [20].

TABLE 1: Clinical and periodontal parameters of three groups.

Characteristics (mean $\pm$ SD)	T2 DM + CP (<i>n</i> = 15)	CP (<i>n</i> = 15)	Healthy (<i>n</i> = 15)		<i>P</i> value
Age (years)	43.33 $\pm$ 10.08	43.87 $\pm$ 7.30	37.53 $\pm$ 6.37		0.070
Gender (M/F)	7/8	8/7	7/8		0.915
BMI (kg/m ²)	24.30 $\pm$ 3.42	23.71 $\pm$ 3.78	21.19 $\pm$ 3.13	T2 DM + CP versus CP	0.644
				T2 DM + CP versus H	0.018
				CP versus H	0.052
HbA1c (%)	7.53 $\pm$ 1.55	5.33 $\pm$ 0.35			<0.001
FBG (mmol/L)	8.69 $\pm$ 3.80	5.41 $\pm$ 0.45	4.92 $\pm$ 0.25	T2 DM + CP versus CP	<0.001
				T2 DM + CP versus H	<0.001
				CP versus H	0.545
PD (mm)	3.52 $\pm$ 0.76	3.93 $\pm$ 0.66	2.18 $\pm$ 0.61	T2 DM + CP versus CP	0.106
				T2 DM + CP versus H	<0.001
				CP versus H	<0.001
AL (mm)	2.78 $\pm$ 1.91	3.29 $\pm$ 1.27	0	T2 DM + CP versus CP	0.297
				T2 DM + CP versus H	<0.001
				CP versus H	<0.001
BI	2.53 $\pm$ 0.77	2.91 $\pm$ 0.75	0.69 $\pm$ 0.46	T2 DM + CP versus CP	0.130
				T2 DM + CP versus H	<0.001
				CP versus H	<0.001

BMI: body mass index; FBG: fasting blood glucose; PD: probing depth; AL: attachment loss; BI: bleeding index.

TABLE 2: Serum leptin and adiponectin levels of three groups.

Characteristics (mean $\pm$ SD)	T2 DM + CP (<i>n</i> = 15)	CP (<i>n</i> = 15)	Healthy (<i>n</i> = 15)		<i>P</i> value
Leptin (ng/mL)	8.30 $\pm$ 2.21	6.46 $\pm$ 1.74	4.46 $\pm$ 1.04	T2 DM + CP versus CP	0.006
				T2 DM + CP versus H	<0.001
				CP versus H	0.003
Adiponectin (μ g/mL)	4.43 $\pm$ 0.96	4.77 $\pm$ 1.10	6.95 $\pm$ 1.21	T2 DM + CP versus CP	0.403
				T2 DM + CP versus H	<0.001
				CP versus H	<0.001
Leptin/adiponectin ratio	1.91 $\pm$ 0.48	1.42 $\pm$ 0.47	0.65 $\pm$ 0.13	T2 DM + CP versus CP	0.002
				T2 DM + CP versus H	<0.001
				CP versus H	<0.001

TABLE 3: Results of Spearman rank correlation coefficient test.

Characteristics	Leptin		Adiponectin		L/A ratio	
	<i>r</i>	<i>P</i>	<i>r</i>	<i>P</i>	<i>r</i>	<i>P</i>
PD	0.420	0.004	-0.543	0.002	0.508	<0.001
AL	0.565	<0.001	-0.484	0.001	0.610	<0.001
BI	0.559	<0.001	-0.501	<0.001	0.609	<0.001

PD: probing depth; AL: attachment loss; BI: bleeding index.

In our present study, patients in CP group had higher level of leptin, lower level of adiponectin, and higher leptin/adiponectin ratio in serum than healthy people, while patients in T2 DM + CP group had even higher level of leptin and similar level of adiponectin compared to CP group, and their ratio of leptin/adiponectin was the highest among

three groups, which meant that chronic periodontitis could influence the level of adipokines in serum and change the leptin/adiponectin ratio, and the effect would be enhanced combining with type 2 diabetes.

Adiponectin has insulin-sensitizing and anti-inflammatory properties [2]. It inhibits IL-6 and TNF- α production

by macrophages and increases the production of important anti-inflammatory factors such as IL-10 or IL-1RA by human monocytes, macrophages, and dendritic cells [21].

leptin plays an important role in the process of insulin sensitivity regulation and could be a proinflammatory factor [2]. It stimulates the immune system by enhancing proinflammatory cytokine production and phagocytosis by macrophages [11]. Therefore, during infection and inflammation, leptin expression is modulated in a manner similar to the cytokine response to infection and injury and could increase in some inflammatory diseases such as periodontitis [22, 23].

According to the different properties of adiponectin and leptin, some researches recently found that the ratio of leptin/adiponectin could be a useful index of insulin resistance [13–16]. The ratio of leptin/adiponectin correlates with glucose infusion rate (GIR) more closely than leptin and adiponectin alone or HOMA-R [16].

The inflammatory mechanism has now been considered to be an important part of the pathogen of diabetes and be closely linked with insulin resistance. The increasing of inflammatory cytokines such as TNF- α , IL-1 β , and IL-6 could impair insulin signaling pathways as well as reduce the function of mitochondria and result in insulin resistance [24].

In our investigation, strong correlations were observed between the ratio of leptin/adiponectin and periodontal parameters. This phenomenon suggests potential relationship between periodontal inflammation and insulin resistance while further studies in larger populations are required.

5. Conclusion

In conclusion, chronic periodontitis could influence the level of adipokines in serum and change the ratio of leptin/adiponectin, and the effect would be enhanced combining with type 2 diabetes. What is more, the ratio of leptin/adiponectin had strong positive correlation with periodontal parameters and gave a hint of potential relationship between periodontal inflammation and insulin resistance.

Conflict of Interests

The authors declare that there is no conflict of interests regarding the publication of this paper.

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