Correlation between Visfatin and Creatine Kinase Levels with Periodontal Health Status of Patients with Coronary Atherosclerosis and Chronic Periodontitis

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ABSTRACT

Background: Visfatin is a novel adipokine that mainly secreted by visceral adipose tissue, had an important role in inflammation and immune system. Creatine Kinase (CK) which is an enzyme that is involved in energy metabolism, found in large amounts in myocardium, brain and skeletal tissues.

This study is carried out To evaluate the periodontal health status of the study groups (chronic periodontitis and chronic periodontitis with coronary atherosclerosis) and control groups, to measure the salivary levels of visfatin and Creatine Kinase in these groups and compare between them, and to determine the correlations between salivary visfatin and Creatine Kinase levels with the periodontal parameters in the three groups.

Materials and Methods: eighty participants, males and females were recruited in this study with age ranged from (30-60) years, they were divided into three groups: the first study group was the Chronic periodontitis group (n=30), the second study group was chronic periodontitis and coronary atherosclerosis (n=30) and the control group(n=20) which was healthy systemically with healthy periodontium. Periodontal health status was determined by measuring plaque index(PLI),gingival index (GI), probing pocket depth(PPD), bleeding on probing (BOP) and clinical attachment level (CAL),salivary samples were taken from each participants, salivary visfatin levels were determined by enzyme-linked immune-sorbent assay(ELISA) while the activity of salivary Creatine Kinase was determined spectrometrically by using the International Federation of the Clinical Chemistry (IFCC) method on Hitachi 911 Automatic analyzer.

Results: The results of the study showed that the mean values of PLI, GI, visfatin, Creatine Kinase and the percentages of sites according to PPD scores, CAL scores, BOP were higher in the second study group with chronic periodontitis and coronary atherosclerosis than in the other groups with highly significant differences between the groups at (P≤0.01). Also by using Pearson Correlation Coefficient, salivary visfatin levels were correlated positively with all clinical periodontal parameters with a strong and positive correlation between salivary visfatin levels and CAL scores and PPD scores. Salivary Creatine Kinase levels were correlated positively with all clinical periodontal parameters with a strong and positive correlation between its levels and mean values of GI and percentages of BOP.

Conclusion: The present study showed that salivary visfatin can be used as a marker for the development of coronary atherosclerosis and its levels are associated with the degree of periodontal destruction and showed that Creatine Kinase may be used as a marker for coronary atherosclerosis and chronic periodontitis.

Keywords: Visfatin, Creatine Kinase, Periodontitis, Atherosclerosis. (J Bagh Coll Dentistry 2016; 28(3):121-125).

INTRODUCTION

Chronic periodontitis is one of the most commonly occurring disease in human which had profound effect on person health [1]. It is considered as a major health problem that if left untreated may become a risk factor for many systemic diseases such as cardiovascular disease [2].

Although the development of periodontitis require the presence of bacteria, it also require the presence of susceptible host, host response is usually mediated by neutrophil cells, lymphocyte and macrophage [3].

These cells were stimulated to produce many cytokines and enzymes that contribute to further tissue destruction [4].Coronary artery disease is the most common type of heart diseases, coronary atherosclerosis which occur as a result of narrow-ing and hardening of the arteries that supply the heart as a result of build of atherosclerotic plaque [5].

It is characterized by local and systemic host responses as cells such as B and T lymphocyte and macrophage which had an important role in the pathogenesis of this disease by secretion of cytokines and enzymes [6].

The presence of inflammatory source in the oral cavity may worsen the atherosclerotic process by stimulation of cellular and humoral mediated immune response [7].

The possible linking mechanisms between periodontitis and coronary atherosclerosis are by sharing the same risk factors, role of immune cells, increase in WBC counts, inflammatory mediators and the role of bacterial lipopolysaccharides [8].

Adipose tissue is the main site for lipid storage, there are two types of adipose tissue, white and brown adipose tissue. The adipose tissue release many biologic active proteins with low molecular weight, these were named as

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adipokines [9]. These adipokines are important in lipid and glucosehoemostasis and many other functions [10].

One of the newly discovered adipokines is visfatin (Visceral fat cytokine), which is 52 kilodalton (kDa) protein. Visfatin was first describedaspre-B cell colony enhancing factor and Nicotinamide phosphoribosyl transferase (NAMPT) because it is involved in nicotinamide adeninedinucleotide synthesis from nicotinamide [11], it has insulin-mimetic properties [12].

Visfatin role in immunity was explained as its gene was expressed in lymphocyte cells and it also induced the production of interlukins such as IL-1B,IL-6 and Tumor necrosis factor which are pro-inflammatory cytokines and IL-1α and IL-10 which are anti-inflammatory cytokines [13] ,and it had an important roles in metabolism, aging and inflammation [14].

There is a direct association between visfatin levels and increased cardiovascular disease [15] and it had a role in many pathophysiological processes that eventually lead to cardiovascular disease such as hypertension and atherosclerosis. However, whether visfatin is a friend or not in these diseases remain unclear [16].

Visfatin concentrations increased with the severity of periodontal diseases from healthy periodontium to gingivitis to periodontitis [17]. Creatine Kinase (CK) is 82 kDa enzyme that found mainly in tissue with high energy demands especially skeletal muscle, brain and myocardium [18]. The increased levels of serum CK were associated with muscle disruption, cell damage and necrosis [19]. It was considered as a marker of cardiovascular disease [20], it was also used to detect periodontal diseases and determine the success of periodontal treatment [21].

Because there is no information about visfatin levels in saliva of patients with coronary atherosclerosis and its association with its levels in chronic periodontitis, therefore, it was decided to conduct this study.

MATERIALS AND METHODS

The study sample was consisted of eighty participants with age range of (30-60) years from both genders. The participants recruited for the study were patients who attended to Baghdad Teaching Hospital, Iraqi centre for heart diseases in GhazyAl-Harery Hospital for catheterization as well as patients from the department of Periodontics in the teaching hospital of College of Dentistry, University of Baghdad.

All participants were informed about the aims of the study orally and by written as a written informed consent was assigned by all participants. The participants were divided into three groups:

1. Study group I (CP):- consisted of thirty participants with chronic periodontitis only without history of any systemic diseases.(patients with chronic periodontitis should have at least 4 sites with pocket depths ≥4mm with clinical attachment loss of(1-2)mm or greater ,this was measured according to Lang et al [22].

2. Study group II (CP+CA):-consisted of thirty patients with chronic periodontitis and coronary atherosclerosis (C.A) who had heart attack since no more than six months and diagnosed for C.A by catheterization and they were on (plavix drug 75 mg)they should have at least 4 sites with pocket depths ≥4mm with clinical attachment loss of(1-2)mm or greater, this was measured according to Lang et al [22]admitted to Iraqi center for heart diseases for treatment.

3. Control group: consisted of twenty patients who were healthy systemically and periodontally.

Sample of 5mL of whole unstimulated saliva was taken from each patient. Following this full examination of clinical periodontal parameters (PLI, GI, BOP, PPD and CAL) was done by

1. Assessment of soft deposits by Plaque index system by Silness and Loe [23].

2. Assessment of Gingival Inflammation by Gingival index system by Loe [24]

3. Assessment of Bleeding on probing according to Salvi [25].

4. Assessment of Probing Pocket Depth by Salvi [25]. A scale was designed for ease of estimation.

Score 0: 1-3 mm

Score1: 4-5mm

Score 2: 6mm and greater

5. Assessment of Clinical attachment level by [26] CAL readings were divided into 3 scores [27].

Score 1: 1-2 mm

Score2: 3-4 mm

Score 3: 5mm and greater

Saliva was centrifuged at 2000 r.p.m for ten minutes, the resultant supernatant was aspirated and, then put into two eppendorff tubes (one for visfatin Elisa kit and the other for Creatine Kinase kit)and kept frozenat -20ºC until analyzed.

Salivary visfatin level was determined by the enzyme-linked immune-sorbent assay(ELISA) in the teaching laboratory of medical city in Baghdad while the activity of salivary CK was determined spectrometrically by using the International Federation of the Clinical Chemistry (IFCC) method on Hitachi 911 Automatic analyzerin the laboratory of poison centre of the specialized surgeries hospital.

Statistical analysis was done using mean, SD, percentages, ANOVA test, chi-square test, and correlation coefficient (r).

RESULTS

The present study showed that the study CP+CA group had the highest mean value of PLI and GI among the three groups (as shown in table 1), the mean and SD were (2.48±0.17), (2.2±0.15) then followed by CP group, the mean and SD were (2.08±0.52), (1.6±0.38),and finally the control group showed the lowest mean and SD (0.1±0.04), (0.07±0.03). Also in table 1, percentages of bleeding on probing sites were higher in CP+CA group than in CP group which were 83.56% and 52.7 % respectively.

Regarding PPD scores, it was clearly shown in table 2 that the numbers and percentages of sites with score 1 and score 2 were higher in CP+CA group than in CP group while the number and percentages of sites with score 0 were higher in CP group than in CP+CA with highly significant

differences at P<0.01 when Chi-square test was applied for comparison (as shown in table 3).

Table 2 also showed that the numbers and percentages ofsites with score 2 of CAL and score 3 were higher in CP+CA group than in CP group while the number and percentages of sites with score 1 were higher in CP group than in CP+CA with highly significant differences at P<0.01 when Chi-square test was applied for comparison as shown in table 3. The analysis of Visfatin and CK in table 4 showed that the study CP+CA group with the highest mean value among the groups of the study, the mean and SD were (1052.4±132.4) for visfatin and (11.55±1.3) for CK and then followed by CP group (457.8±208.7) and (4.94380±1.4), and finally the control group with the mean and SD (0.62±0.2), (1.6±0.2)which had the lowest mean value. Salivary Visfatin and Creatine Kinase levels were correlated positively with the mean values of GI and percentages of BOP as shown in table 5. Also salivary visfatin levels were correlated positively and strongly with all PPD scores (as shown in table 6) and CAL scores as shown in table 7.

Table 1:The mean values and Standard deviation of PLI and GI and the percentages of sites with BOP among the groups

Groups	PLI		GI		BOP	
	Mean	SD	Mean	SD	Score 0	Score 1
CP	2.0827	0.5	1.62800	0.3	47.3%	52.7%
CP+CA	2.4833	0.1	2.22000	0.1	16.44%	83.56%
Control	0.1094	0.04	0.07010	0.03		

Table 2:Number and percentages of sites according to PPD and CAL for the study groups

Group	PPD						CAL					
	Score 1		Score2		Score3		Score 1		Score 2		Score 3	
	NO	%	NO	%	NO	%	NO	%	NO	%	NO	%
CP	439	15	2337	79.9	146	4.9	1169	40	1461	50	292	10
CP+CA	30	1	2767	94	147	5	294	9.9	2356	80.2	294	9.9

Table 3:Comparison between study groups according to PPD and CAL Scores

Group	Chi-square test		P-value		Sig	
	PPD	CAL	PPD	CAL	PPD	CAL
CP	392.83	733.12	<0.0001	<0.0001	HS	HS
CP+CA						

Table 4: The mean values of salivary visfatin and CK among the groups of the study

Groups	Visfatin		CK	
	Mean	SD	Mean	SD
CP	457.8	208.7	4.94380	1.4
CP+CA	1052.4	132.4	11.55	1.3
Control	0.62	0.2	1.6	0.2

Table 5: Pearson's correlation coefficient (r) between visfatin and CK with periodontal parameters (PLI,GI,BOP).

Visfatin	PLI			GI			BOP		
	r	P-value	Sig	r	P-value	Sig	r	P-value	Sig
CP	0.4	0.01	HS	0.1	0.49	NS	0.002	0.9	NS
CP+CA	0.7	0.000	HS	0.5	0.003	HS	0.14	0.4	NS
Control	0.9	0.000	HS	0.7	0.000	HS			
CK									
CP	0.4	0.009	HS	0.9	0.000	HS	0.7	0.000	HS
CP+CA	0.6	0.000	HS	0.9	0.000	HS	0.5	0.004	HS
Control	0.2	0.38	NS	0.2	0.3				

Table 6: Pearson's Correlation Coefficient (r) between PPD Scores and the levels of salivary CK enzyme and visfatin for each study group

Parameter	Groups	Scores		r	P-value	Sig
PPD	CP	Score 0	Visfatin	0.793	0.000	HS
			CK	0.04	0.8	NS
		Score 1	Visfatin	0.9	0.000	HS
			CK	0.137	0.471	NS
		Score 2	Visfatin	0.754	0.000	HS
			CK	0.03	0.85	NS
	CP+CA	Score 0	Visfatin	0.12	0.52	NS
			CK	0.26	0.15	NS
		Score 1	Visfatin	0.73	0.000	HS
			CK	0.01	0.95	NS
		Score 2	Visfatin	0.74	0.000	HS
			CK	0.397	0.03	NS

Table 7: Pearson's Correlation Coefficient (r) between CAL and the levels of salivary CK enzyme and visfatin for each study group

Parameter	Groups	Scores		r	P-value	Sig
CAL	CP	Score 1	Visfatin	0.56	0.001	HS
			CK	0.09	0.6	NS
		Score 2	Visfatin	0.79	0.000	HS
			CK	0.09	0.6	NS
		Score 3	Visfatin	0.602	0.000	HS
			CK	0.11	0.5	NS
	CP+CA	Score 1	Visfatin	0.893	0.000	HS
			CK	0.17	0.35	NS
		Score 2	Visfatin	0.92	0.000	HS
			CK	0.28	0.12	NS
		Score 3	Visfatin	0.89	0.000	HS
			CK	0.2	0.3	NS

DISCUSSION

Periodontitis and Coronary atherosclerosis are multi-factorial diseases with an onset in early childhood while their manifestation may appear in adulthood [28].These two entities affect each other as cardiovascular diseases is one of the most important diseases caused or exacerbated as a result of periodontal disease .Both of these diseases lead to the release of inflammatory mediators from the damaged tissue into saliva and other biological fluid [29].

The mean values of PLI, GI, visfatin, Creatine Kinase and the percentages of sites according to PPD scores, CAL scores, BOP were higher in the second study group with chronic periodontitis and coronary atherosclerosis than in the other groups with highly significant differences between the groups at ($P \leq 0.01$).

Visfatin play a role in increasing the expression of pro-inflammatory cytokines such as TNF α and MMP and other biomarkers in response to the presence of inflammation [30]. CK is an intracellular enzyme that participates in many metabolic processes in the cells of tissue

and it was released in large amount from the damaged cells of periodontal tissue in response to inflammation and it is considered as a reflection of metabolic changes in the gingiva and periodontium during inflammation [31].

The results of this study showed that there was an increase in salivary visfatin and CK levels with the presence of periodontitis and coronary atherosclerosis. It was also established a strong positive correlation between CK activity and the mean values of GI and percentages of BOP and a strong and a positive correlation between visfatin levels and PPD and CAL scores.

In a conclusion, CK and visfatin can be used as a marker of periodontitis and C.A so it may contribute in identification of higher risk individuals as well as lead to new therapeutic approach.

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