Relationship between periodontal diseases and C-reactive protein among hypertensive patients under β-blocker antihypertensive drug
(Clinical and Biochemical study)

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ABSTRACT

Background: Hypertension is the most important public health problem in the world and one of the major risk factors for cardiovascular diseases, and it has been reported that hypertension is linked with periodontal diseases and both condition have reported to elevated levels of C-reactive protein.

Aims of the study: To determine the periodontal health status and the concentration of C-reactive protein in saliva among patients with hypertension and under β-blocker treatment and to compare the results with systemic healthy individuals, also to correlate the clinical findings with biochemical findings.

Materials and Methods: Test group consist of 25 hypertensive patients and under β-blocker treatment{Atenolol(Tenormin) 50 mg/day}, the test group further subdivided into three groups according to the duration of medication into: test I group under medication less than one year, test II group under medication between one to four years, test III group under medication more than four years.In addition to25 control group. Their age was between (40-45) years and all patients in both groups were male and non-smokers. Periodontal disease was evaluated by recording the plaque index, gingival index, bleeding on probing, probing pocket depth and clinical attachment level. Unstimulated salivary samples were collected and then chemically analyzed using high sensitivity ELISA to determine the concentration of C-reactive protein.
Results: The mean value of all recorded periodontal parameters were highest among test group compared to control with statistically significant difference existed between both groups($p=0.001$) for plaque index, ($p=0.008$) for gingival index, ($p=0.006$) for bleeding on probing, ($p=0.017$) for probing pocket depth, ($p=0.002$) for clinical attachment level.
In regard to the concentration of salivary C-reactive protein, the mean value was highest among test group compared to control with statistically non-significant differences between both groups($p=0.606$).

The correlation coefficient between salivary C-reactive protein and periodontal parameters showed statistically non-significant correlation in both test group and control. Among test group, result revealed statistically significant correlation between salivary C-reactive protein and pocket depth among test group III (under medication more than four years)($p=0.039$).

Conclusion: The study revealed poor condition of the oral cavities regarding the periodontal condition of patients with hypertension, so the co-operation between general practitioners, cardiologists and dentists needs to be intensified. The concentrationsof salivary C-reactive protein of test groups were higher than control.
Key words: Periodontal diseases, hypertension, C-reactive protein

INTRODUCTION

Periodontium is a complex and highly specialized pressure-sensing system consisting of four tissues (cementum, periodontal ligament, alveolar bone, and junctional and sulcular epithelia) supporting the teeth. Of these structures, periodontal ligament is a dynamic tissue with a high rate of remodeling and turnover, which connects the teeth to the alveolar bone [1]. Periodontal disease is defined as a chronic inflammatory disease of teeth-supporting tissues. The spreading of the inflammatory process from the gingiva deep into periodontium tissues may lead to the destruction of the alveolodental ligament and considerable bone loss in the alveolar process. Although the primary cause of periodontitis is bacterial infection, several systemic diseases seem to be associated with the development of destructive periodontal disease [2].

Hypertension is one of the most important risk factors for strok, myocardial infarction, peripheral vascular disease, heart failure, and end-stage renal disease. Hypertension is a major global public health problem. It is affects approximately one billion people worldwide and estimated that about 26.4% of global adult population have hypertension with two third of them living in economically developing nations [3-4-5].Despite the general agreement that arterial hypertension is a significant risk factor for cardiovascular diseases. Recent evidence have linked periodontal diseases with high blood pressure [6-7]. Other measures of poor oral health (tooth loss) have been associated with hypertension [8].The rational for an association between hypertension and periodontal disease is based on findings showing that hypertension leads to morphological changes of vessels feeding the periodontal membrane, affecting the position of the tooth [9].

Saliva is very important body fluid often taken for

granted. It is critical to the maintenance of oral health. Saliva has also become useful as a non-invasive alternative for blood in medical diagnosis and research [10].

C-reactive protein (CRP) is a non-specific inflammatory marker present in the blood and saliva and commonly used in paediatrics in the diagnosis and monitoring of inflammation and active infection, as C-reactive protein values increase markedly during these acute processes. C-reactive protein elevated in hypertension, and elevated among those with periodontal diseases [11-12-13]. High sensitivity methods have recently been developed and permit the determination of CRP levels far below those found in inflammatory processes [14].

MATERIALS AND METHODS

sample

Study group consisted of (25 males, non-smokers) with confirmed diagnosis of hypertension under medication (which include only those patients under β-blocker {Atenolol(Tenormin) 50 mg / day}. Patients under other types of medication and/or with any other systemic disease were excluded from this study. Their age was ranged between (40-45 years). A control group of (25 males, non-smokers and without any systemic diseases) matching with age of study group was also examined.

1-Periodontal clinical examination

Periodontal clinical parameters were carried out for all permanent teeth and four surfaces of each tooth were scored by using mouth mirror, diagnostic probe, and periodontal probes. The following indices were recorded:

A.Plaque index [15]
By using dental mirror and diagnostic probe and before salivary sample collection, the criteria for this index:

Score 0: Absence of plaque deposits

Score 1: Plaque disclosed after running the periodontal probe along the gingival margin.

Score 2: Moderate accumulation of plaque not exceeding one third of tooth surface and can be detected by naked eye.

Score 3: Abundance amount of plaque exceeding one third of tooth surface.

B.Gingival index [16]
The criteria of this index are:

Score 0: Entire absence of visual signs of inflammation in the gingival unit.

Score 1: Mild inflammation, slight change in colour, slight edema, no bleeding on probing.

Score 2: Moderate inflammation, moderate glazing, redness, edema and hypertrophy, bleeding on probing.

Score 3: Sever inflammation, marked redness and hypertrophy ulceration, tendency to spontaneous bleeding.

C.Bleeding on Probing

The four surfaces of each permanent teeth were evaluated by running the periodontal probe gently inside the gingival sulcus, If bleeding occurs within 30 seconds after probing, the site was given a positive score, and a negative score is given for non-bleeding sites .

D.Probing Pocket Depth

The distance from the gingival margin to the location of the tip of a periodontal probe inserted in the pocket with moderate probing force was recorded by at four surfaces of all examined permanent teeth.

E. Clinical Attachment Level (*Ramfjord 1959*)
The distance from the cemento-enamel junction (CEJ) to the location of the inserted probe tip was measured at four surfaces of all examined teeth. Loss of attachment was done according to Ramfjord by:

- Measuring the distance from the free gingival margin to the bottom of the gingival sulcus .The interproximal recording done at the buccal aspect of the inter proximal contact.
- Measuring the distance from the free gingival margin to the cemento-enamel junction.
- The attachment loss was obtained from subtracting the above two Measurement.
- Loss of attachment in case of gum recession was recorded by adding the first measurement to the second one.

2-Biochemical analysis

Whole saliva was collected by tilting the head forward, allowing the saliva to pool on the floor of the mouth, then passing the saliva into a disposable test tube, Samples visibly contaminated with blood were recollected. Sample collection within 60 minutes after eating a major meal was avoided because acidic or high sugar foods can compromise assay performance by lowering sample pH and influencing bacterial growth and to minimize these factors, rinse mouth thoroughly with water before sample was collected. After collection the samples keep cold, in order to avoid bacterial growth and loss of CRP in the specimen and all samples were freezed below -20ºC as soon as possible after collection. Freezed saliva samples will precipitate the mucins. On day of assay, thaw completely and centrifuge at 3000 rpm for 15 minutes then subjected to biochemical analysis to determine the concentration of C-reactive protein using ELISA .

RESULTS

Results of salivary C-reactive protein are illustrated in Table (1).The application of Student's t–test for salivary C-reactive protein revealed a statistically non-significant difference between the test group and control group.

The comparsion of periodontal parameters between the control group and test group has been illustrated in Table (2). The Student's t–test was used and results revealed a statistically significant differences of all periodontal parameter(PlI, GI, BOP, PPD, CAL) between the control group and the test group.

The correlation coefficient between CRP with PlI, GI, BOP, PPD, and CAL, was clarify in Table (3). these results revealed statistically non-significant correlation for both groups. Table (4) demonstrates the correlation coefficient between C-reactive protein with PlI, GI, BOP, PPD, and CAL among the test groups. Results showed a statistically significant correlation of CRP with PPD among test group

DISCUSSION

The mean concentration of C-reactive protein was higher in the saliva of the test group than the control group the explanation of this result was due to that hypertension increase the level of salivary C-reactive protein, this result agree with previous stud which shown that C-reactive protein is positively associated with hypertension [17-18]. For periodontal parameters, the mean for plaque index in test group was higher than the control group The possible explanation of such results may be due to that people with hypertension neglect the oral hygiene measures and did not brush their teeth regularly.This result agree with previous study [19]. Results of the GI and BOP in the present study showed that mean of these indices were higher among test group than control, and a statistically significant differences between the test group and control group This result coincid with previous study [20]. Regarding the PPD and CAL, the present study clarified that the mean of these parameters were higher in test group than control group and results illustrated significant differences between them, these finding are in concordant with many studies which has shown that high blood pressure was significantly associated with the prevalence of 5 millimetres or deeper periodontal pockets, and loss of attachment [21-22]., Suggested potential mechanisms linking periodontal inflammation with BP may be refered to a direct effect on endothelial dysfunction or an indirect stimulation of a systemic metabolic/inflammatory host response. For correlation coefficient of salivary C-reactive protein with periodontal parameters, it was only significantly correlated to pocket depth (p < 0.039)in test group III, this may be due to the increase in surface area for bacteria, plaque, and calculus to inflict a chronic infection, while the results of correlation coefficient between salivary C-reactive protein and the remaining periodontal parameters in both test and control groups were non- significant. These finding were supported by [13-23] who demonstrated a positive correlation between C-reactive protein and severity of periodontal disease.

Table 1:

Control Group		Test Group		t–value	p–value
Mean	+ SD	Mean	+ SD		
1867.7948	1307.7668	2084.1978	1624.2753	–0.519	0.606

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Table 2:

Parameters	Control Group		Test Group		t–value	p–value
	Mean	+ SD	Mean	+ SD		
PlI	0.77552	0.529025	1.30608	0.560560	−3.442	0.001*
GI	0.66104	0.508803	1.09744	0.603545	−2.764	0.008*
BOP	0.14528	0.212398	0.37268	0.330381	−2.895	0.006*
PPD(mm)	3.75444	1.436294	4.48116	0.302877	−2.475	0.017*
CAL(mm)	2.17204	0.720295	2.70228	0.367945	−3.278	0.002*

Table 3:

Parameter	CRP (pg/ml)			
	Control Group		Test Group	
	r–value	p–value	r–value	p–value
PlI	0.102	0.626	0.300	0.145
GI	0.132	0.528	0.271	0.189
BOP	−0.020	0.924	0.323	0.115
PPD (mm)	−0.031	0.884	−0.063	0.764
CAL (mm)	−0.194	0.354	0.223	0.283

Table 4:

Parameter	CRP (pg/ml)					
	Test I Group		Test II Group		Test III Group	
	r–value	p–value	r–value	p–value	r–value	p–value
PlI	0.243	0.562	−0.579	0.133	0.626	0.071
GI	0.438	0.278	−0.566	0.144	0.536	0.137
BOP	0.337	0.414	−0.473	0.236	0.598	0.089
PPD (mm)	−0.477	0.232	−0.582	0.130	0.692	0.039*
CAL(mm)	0.273	0.513	−0.200	0.635	0.444	0.232

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REFERENCES

1. Benigeri M, BrodeurJM, Payette M, Charbonneau A, Ismail A I. Community periodontal index of treatment needs and prevalence of periodontal conditions. J Clin Periodontol 2000 ;27: 308–312.

2. Hung H-C, Willett W, Merchant A, Rosner BA, Ascherio A, Joshipura K J. Oral health and peripheral arterial disease. Circulation 2003; 107:1152–1157.

3. Kearney PM, Whelton M, Reynolds K, Whelton PK, He J. Worldwide prevalence of hypertension: a systematic review. J Hypertens 2004; 22: 11–19.

4. Kearney PM, Whelton M, Reynolds K, Muntner P, Whelton PK, He J. Global burden of hypertension: analysis of worldwide data. Lancet 2005; 365:217–23.

5. Hajjar I, Kotchen JM, Kotchen TA . Hypertension: trend in prevalence, incidence and control .Annu Rev Public Health 2006; 27:465-90.

6. Inoue, K., Kobayashi, Y., Hanamura, H. , Toyokawa, S. Association of periodontitis with increased white blood cell count and blood pressure. Blood Pressure 2005; 14: 53–58.

7. Borges-Ya´n˜ez, S. A., Irigoyen-Camacho, M. E. , Maupome´, G. Risk factors and prevalence of periodontitis in community-dwelling elders in Mexico. Journal of Clinical Periodontology 2006; 33: 184–194.

8. Vo¨lzke H,Schwahn C, Do¨rr M,Aumann N, Felix S B, John U, Rettig R, Do¨ren M,Biffar R, Kocher T. Inverse association between number of teeth and left ventricular mass in women. Journal of Hypertension2007; 25: 2035–2043.

9. Ioi H,Nakata S,Nakasima A, Counts AL, Nanda RS . Changes in tooth position in humans in relation to arterial blood pressure. Arch Oral Biol 2002; 47:219–226.

10. Aps J K M, Martens L C. Review: the physiology of saliva and transfer of drug into saliva. Forensic SciInt 2005; 150:119-31.

11. Loos BG, Craandijk J, Hoek FJ, Wertheim-van Dillen PM, van der Velden U. Elevation of systemic markers related to cardiovascular diseases in the peripheral blood of periodontitis patients. J Periodontol 2000 ;10:1528-1534.

12. Kiechl S, Egger G, Mayr M, et al. Chronic infections and the risk of carotid atherosclerosis: Prospective results from a large population study. Circulation 2001;103;8:1064- 1070.

13. Noack B, Genco RJ, Trevisan M, Grossi S, Zambon JJ, et al. . Periodontal infections contribute to elevated systemic C-reactive protein level. J Periodontol 2001; 72;9:1221-1227.

14. Ford ES, Giles WH, Myers GL, et al . C-reactive protein concentration distribution among US children and young adults: findings from the National Health and Nutrition Examination Survey, 1999–2000. ClinChem 2003 ; 49:1353–7.

15. Silness J, Loe H. Periodontal disease in pregnancy (II): Correlation between oral hygiene and periodontal conditions. Octa Odontol Scand 1964; 22:121-35.

16. Loe H, Silness J. Periodontal disease in pregnancy I. Prevalence and severity. Octa Odontol Scand 1963;21:533-551

17. Sesso HD, Buring JE, Rifai N, Blake GJ, Gaziano JM, Ridker PM. C-reactive protein and the risk of developinghypertension. JAMA 2003; 290: 2945–2951.

18. Sung KC, Suh JY, Kim BS, Kang JH, Kim H, Lee MH, Park JR, Kim SW. High sensitivity C-reactive protein as an independent risk factor for essential hypertension. Am J Hypertens.2003 ;16:429–433.

19. Valentaviciene G, Anuseviciene OV, Paipaliene P, Nedzelskiene I .Oral Health Status in the Participants of the"Juvenile Hypertension Program 2002"Stomatologija, Baltic Dental and Maxillofacial Journal 2004; 6:24-27.

20. TsakosG, Sabbah W, Hingorani AD, Netuveli G, Donos N, Watt RG, et al . Is periodontal inflammation associated with raised blood pressure? Evidence from a National US survey. J Hypertens 2010; 28:2386–2393.

21. Holmlund A, Holm G, Lind L. Severity of periodontal disease and number of remaining teeth are related to the prevalence of myocardial infarction and hypertension in a study based on 4,254 subjects. J Periodontol 2006;77:1173-1178.

22. Engstrom S, Gahnberg L, Hogberg H, Svardsudd K. Association between high blood pressure and deep periodontal pockets: a nested case-referent study. Ups J Med Sci 2007;112:95-103.

23. Al-Safi A. Biochemical, Immunological and Histochemical study of cyclosporine-A induced gingival enlargement in kidney transplanted patients. A Ph.D Thesis. *College of Dentistry, University of Baghdad.2007; P:54-56.*