An Assessment of Oral Health in Hypertensive Patients Treated with HMG-CoA Reductase Inhibitors (Statins)

Amir A. M. Al-Joboury, B.D.S. [(1)]
Rafil H. Rasheed, B.D.S., M.Sc. [(2)]

ABSTRACT

Background: Hypertension is a chronic medical condition in which the blood pressure in the arteries is elevated, it's classified as either primary (essential) hypertension or secondary hypertension, and it increases the risk of ischemic heart disease, peripheral vascular disease and other cardiovascular diseases. Several classes of medications collectively referred to as antihypertensive drugs like beta blockers, calcium channel blockers, angiotensin converting enzyme (ACE) inhibitors, angiotensin receptor blockers, renin inhibitors and statins (HMG-CoA) reductase inhibitor. Statin medication may have some beneficial effects when subjects have dental plaque or signs of periodontitis as gingival bleeding. The purpose of this study were to assess the oral health in hypertensive patients are treated with statins in terms of salivary flow rate, pH and oral health indices.

Materials and Methods: Ninety saliva specimens collected from three groups of subjects (thirty healthy patients "control" Group I), thirty hypertensive patients treated with anti-hypertensive medications without taking statins (Group II) and thirty hypertensive patients treated with anti-hypertensive medications with statins (Group III). Unstimulated saliva was collected from each patients and participants for assessment of salivary flow rate and salivary pH.

Results: Salivary flow rate is reduced in Group II and III patients compared with Group I. Significant low salivary flow rate observed in Group III patients (hypertensive treated with statins) compared with Group II (hypertensive untreated with statins) and Group I (healthy subjects); The median value of gingival index is significantly higher in Group II compared with corresponding value in Group I, while it attended a significant low value in Group III patients; There is no significant difference in DMF score between Group I and Group III, while a significant high score observed in Group II compared with Group I ; The percent of carries restoration in patients of Group II is significantly low compared with corresponding value of Group I . Although the percent of carries restoration in patients of Group III is less than corresponding value of Group I but it does not reach significant level.

Conclusions: Patients using statins therapy are more likely have an improvement in gingival index, DMF score and carries restoration. The salivary flow rate is reduced in patients treated with statins medications, statins therapy have a beneficial effect on the oral cavity.

Key words: Oral health, Hypertension, Statins, Salivary flow rate. (J Bagh Coll Dentistry 2015; 27(4):85-89).

INTRODUCTION

Hypertension or high blood pressure is a chronic medical condition in which the blood pressure in the arteries is elevated.[(1)] Blood pressure is summarized by twomeasurements, systolic and diastolic, which depend onwhether the heart muscle is contracting (systole) or relaxedbetween beats (diastole) and equate to a maximum andminimum pressure, respectively. Normal blood pressure atrest is within the range of 100-140mmHg systolic (top reading) and 60-90mmHg diastolic (bottom reading). Highblood pressure is said to be present if it is persistently at orabove 140/90 mmHg. Hypertension puts persistent strain on the heart, leading tohypertensive heart disease and coronary artery disease ifuntreated.

Hypertension is also a major risk factor forstroke, aneurysms of the arteries (e.g. aortic aneurysm), peripheral arterial disease and is a cause of chronic kidney disease. Dietary and lifestyle changes can improve blood pressure control and decrease the risk ofassociated health complications, although drug treatment is often necessary in people for whom lifestylechanges are not enough or not effective[(2)]. Subsequently, beta blockers, calcium channel blockers, angiotensin converting enzyme (ACE) inhibitors, angiotensin receptor blockers and HMG-CoA reductase inhibitors (statins) were developed as antihypertensive agents.[(3)]

Statins are hydoxy-3 methyl-glutaryl-CoA (HMG-CoA) redctase competitive inhibitors are commonly used in management of cardiovascular diseases in presences or absence the risk factor that related to abnormal lipid profile. There is no doubt that there is a link between bad oral health and cardiovascular diseases particularly coronary artery disease[(4)]. Statins have been found to prevent cardiovasculardisease in those who are at high risk: researchers found that statins are most effective for treating cardiovasculardisease (CVD) as a secondary prevention strategy (treatment in the early stages of a disease), however, benefitin those with elevated cholesterol levels but without previous CVD is questionable[(5)].

It was shown that patients on statin medication exhibited reduced periodontal injury as compared to subjects without the drugs[(6)]. Statin medication may have some beneficial effects when subjects

(1)Master student. Department of Oral Diagnosis. College of Dentistry, University of Baghdad.
(2)Professor. Department of Oral Diagnosis. College of Dentistry, University of Baghdad.

have dental plaque or signs of periodontitis as gingival bleeding[4]. Furthermore, it is previously reported that statins have an effect on the salivary flow, they reduced the unstimulated salivary flow[7].

MATEREALS AND METHODS

The present study conducted in Department of Oral Diagnosis, College of Dentistry, The University of Baghdad, Iraq from November 2013 till May 2014. Approved by the Scientific Committee in the institution and a consent form was obtained from each participant who enrolled in the study. The patients were recruited from the General Medicine Clinic in the Primary Health Centre at Al-Shirqat district area in Sallahalden governorate, and general medicine private clinics.

The eligible patients are both gender of age (50-60) years old, presented with hypertension and they were under treatment with anti-hypertensive agents and/or with statins. The antihypertensive medications that used by patients are: Atenolol, Captopril, Diltiazem, Bisoprolol, Losartan, Aspirin, Aldomet, Diovan, Lisnopril. The statins that used by patients are: Atorvastatin, Simvastatin, Fluvastatin, Rosuvastatin.

The criteria of exclusion included; pregnancy and lactated mothers, chronic liver disease. Diabetes mellitus, renal failure, recent infections and patients on the antisteroidal anti-inflammatory drugs (within two weeks before enrolled in the study).A total number of ninety patients are in rolled in the present study.

They are grouped into: Group I (n=30): Control group, healthy subjects; Group II (n=30): Hypertensive patients without taking statins; Group III (n=30): Hypertensive patients with statinsA demographic, medical and oral hygiene data are obtained from each patient. The demographic characteristic of patients included: gender, age, medical history, oral health, and history of the disease, current drug intake, duration of intake, status of intake (regular or irregular). Then the patients were examined thoroughly taking in consideration the variables that involved in the current research.

Blood Pressure Measurement:

Arterial pressure is most commonly measured via a sphygmomanometer. Systolic pressure is peak pressure in the arteries, which occurs near the end of the cardiac cycle when the ventricles are contracting. Diastolic pressure is minimum pressure in the arteries, which occurs near the beginning of the cardiac cycle when the ventricles are filled with blood [8].

Oral Examination:

All the patients have been examined orally under standardized conditions. The oral cavity has been examined by artificial light & using a mouth mirror. The examination would begin with the lips, upper and lower sulcus, retro-molar area, upper and lower labial mucosa, buccalmucosa, hard and soft palate, dorsal margin and inferior surface of the tongue, floor of the mouth were also examined. The following are the applied oral assessments:

Gingival index (GI): The GI was proposed by Loe and Silness [9]. The GI is based on two of the characteristic signs of inflammation-swelling (edema) and redness. An important sign is bleeding, it was used to assess the severity of gingivitis. A blunt instrument, such as a periodontal pocket probe, was used to assess the bleeding potential of the tissues. The score of the area around each tooth is calculated, and then the total score of all teeth was divided by the number of teeth. The severity of gingivitis is interpreted as follows: Mild gingivitis = 0.1-1.0; Moderate gingivitis = 1.1 - 2.0; Severe gingivitis = 2.1 - 3.0
Calculation: G.I. = Total scores/ No. of surfaces examined

Decayed-Missing-Filled Index (DMF): This index was introduced by Klein, Palmer and Knutson in 1938 and modified by WHO[10]. The components are: *D component* Used to describe (Decayed teeth), *M component* Used to describe (Missing teeth due to caries), *F component* Used to describe (Filled teeth due to caries). Mean DMF = Total DMF / Total No. of the subjects examined Caries restoration percentage = F / F+D * 100%

Collection of Saliva:

Unstimulated (resting) whole saliva was collected, under resting conditions. Patients were asked to avoid any oral hygienic procedure and rinse their mouth with water and to generate saliva in their mouth and to spit into a wide test tube[11]. The collection period was ten minutes.
SFR (ml/min) = Saliva sample volume (ml) / collection time (min).

The salivary pH was determined by using portable pH-meter (Senso Direct, Germany). The probe of pH meter was immersed in a total volume up to 2 ml salvia and the record of pH was up to the 2 division at the temperature of saliva.

Descriptive inference analysis of the data achieved by application the EXCEL 2007 and SPSS version 17 programs. The data are expressed as number, percent, and whenever possible as mean ± SD and median. Inference

analysis was done by application un-paired two tailed student's t- test taking the probability (p) ≤ 0.05 as the lowest limit of significance.

RESULTS

Characteristics and Medical Measurements:

Table 1 shows the characteristic of the subjects and patients enrolled in the present study. The distribution of patients in Group II shows a low number of male gender in comparison with Groups I and III. There are no significant differences between means of age of the different groups. The habit of smoking is reported in a non-significant low frequency in Group II. Patients of Group III have a significant short duration of disease compared with Group II (2.5±1.2 years versus 7.5±4.4 years, p < 0.001 respectively. Higher number of Group III patients is treated with monotherapy antihypertensive medication compared with Group II (27 versus19 patients out of each 30 patients respectively).

Table 2 shows the measurements of the blood pressure. Systolic, diastolic and mean blood pressures are significantly higher in Groups II and III compared with Group I despite of the antihypertensive drugs that used by patients of Group II and III. Pulse pressure, a measurement of the difference between systolic and diastolic, is significantly higher in Group III compared with group I and II.

Oral Health Indices:

Table 3 shows that the salivary flow rate is reduced in Group II and III patients compared with Group I. Significant low salivary flow rate observed in Group III patients (hypertensive treated with statins) compared with Group II (hypertensive untreated with statins) and Group I (healthy subjects). The salivary pH value is non-significantly increased in Group II compared with Group I while it decreased in Group III compared with Group I or Group II. The median value of gingival index is significantly higher in Group II (1.136) compared with corresponding value in Group I (1.00) while it attended a significant low value (0.419) in Group III patients. There is no significant difference in DMF score between Group I (8.303±4.91) and Group III (10.1±4.9) while a significant high score observed in Group II (12.3±7.2) compared with Group I. The percent of carries restoration in patients of Group II is significantly low (28.5±36.1) compared with corresponding value of Group I (50.8±39.7). Although the percent of carries restoration in patients of Group III (36.1±35.7) is less than corresponding value of Group I but it does not reach significant level.

Table (1): Characteristics of the Study.

	Group I (Healthy Subjects) (n=30)	Group II (Hypertensive patients) (n=30)	Group III (Hypertensive patients treated with statins) (n=30)
Gender (Male: Female)	16:14	8:22	17:13
Age (Year)	54.9±3.1(55)	55.39±3.4(55)	56.2±3.32(57)
Smoking	8	5	8
Alcohol intake	3	2	2
Duration of hypertension (Year)	-	7.5±4.4(7.0)	2.5±1.2(2.2)†
Antihypertensive medication (No.)			
One		19	27
Two		11	3

The results are expressed as number, mean ± SD (median), †p< 0.001 compared with Group II

Table (2): Blood Pressure Measurements.

Blood pressure (mmHg)	Group I (Healthy Subjects) (n=30)	Group II (Hypertensive patients) (n=30)	Group III (Hypertensive patients treated with statins) (n=30)
Systolic	125.9±8.5(87.3)	143.8±13.9(140)*	148.4±15.5(145)*
Diastolic	84.0±8.0(83)	103.2±11.9(100)*	101.0±9.1(100)*
Pulse	42.2±7.9(42.5)	40.7±11.9(40)	47.4±11.3(46.5)**†
Mean	97.7±7.3(96.7)	116.7±11.3(116.7)*	116.8±10.4(115)*

The results are expressed as mean ± SD (median), *p< 0.001, **p< 0.05compared with Group I; †p< 0.05 compared with Group II

Table (3): Assessment of oral Health.

Oral indices	Group I (Healthy Subjects) (n=30)	Group II (Hypertensive patients) (n=30)	Group III (Hypertensive patients treated with statins) (n=30)
Saliva flow rate (ml/min)	0.3660±0.1034(0.37)	0.325±0.0984(0.32)	0.2747±0.0926(0.27)***††
Saliva pH	6.650±0.214(6.635)	6.790±0.368(6.825)	6.450±0.429(6.38)*†
Gingival Index	0.817±0.530(1.00)	1.161±0.601(1.136)*	0.537±0.418(0.419)*†
DMF score	8.303±4.91(7.0)	12.3±7.2(11)**	10.1±4.9(9.5)
Carries restoration (%)	50.8±39.7(43.8)	28.5±36.1(0)*	36.1±35.7(38.8)

The results are expressed as mean ± SD (median), *p< 0.05, **p< 0.01, ***p< 0.001 compared with Group I, †p< 0.001, ††p< 0.05 compared with Group II

DISCUSSION

The results of the present study clearly identified that statins therapy exerts a beneficial effect on the oral cavity by altering the physiochemical property of the saliva, improving the gingival index, DMF score and carries restoration. Therefore, the results of this study can explain by the following points:

1. The characteristics of the study showed that there is no doubt that age factor played a role in the determination the status of the saliva. The mean age of each studied group in current study is comparable and there is no significant differences were observed. This pointed that there is no bias in the results regarding the age factor. The duration of hypertension is more in non-statins group compared with statins treated group which may influence the obtained results. Hypertension itself induced changes in saliva despite the clinical presentation and whatever the medications that used[12]. Therefore, the variation in the duration of hypertension does not impact adversely the results of this study.
2. Blood pressure levels of the present study showed the significant difference between Group II and III in the level of pulse pressure. This observation attributed to the variation in the nature of antihypertensives that used by the patients[13].
3. There is no evidence that lipid lowering agents reduced the pH of saliva. Moreover, the low pH of the saliva in our patients indicating that those patients are not under stress as the increase saliva pH is a marker of stress[14].

Oral Health Indices:

The salivary flow rate is reduced in patients treated with statins. This observation is not agreed the results that showed neither antihypertensive agents nor hypertension as a disease could influence the flow rate or pH of the saliva[12]. It is necessary to mention here that beta-blockers or centrally acting hypertensive's e.g. alpha-methyldopa that caused dry mouth i.e. decrease blood flow[15].

Improvement in the gingival index indicated the favorable effect of statins on the gingiva. This observation is in agreement with other studies that showed statins is useful in chronic periodonitis[16]. The favorable effects of statins on the oral health could be related to the pleiotropic effects that included:

a. Immunomodulatory, antioxidant, antithrombotic and endothelium stabilization actions[17].

b. Promote angiogenesis and increase osteoblastic differentiation[18].

REFERENCES

1. Chobanian AV, Bakris GL, Black HR, Cushman WC, Green LA, Izzo Jr. JL, Jones DW, Materson BJ, Oparil S, Wright Jr. JT, Roccella EJ. Seventh report of the Joint National Committee on Prevention, Detection, Evaluation, and Treatment of High Blood Pressure. Hypertension 2003; 42(6): 1206–52.
2. Carretero OA, Oparil S, et al. Essential hypertension.Part I: definition and etiology. Circulation 2000; 101 (3): 329–35.
3. Chockalingam A. Impact of World Hypertension Day. Canadian J Cardiol 2007; 23(7): 517–9. (IVSL)
4. Saxlin T, Suominen-Taipale L, Knuuttila M, Alha P, Yl¨ostalo P. Dual effect of statin medication on the periodontium. J Clinical Periodontol 2009; 36(12): 997–1003.
5. Taylor F, Ward K, Moore TH et al. Statins for the primary prevention of cardiovascular disease. In Taylor, Fiona. Cochrane Database Syst Rev 2011; 1: CD004816. (IVSL)
6. Lindy O, Suomalainen K, Makela M, Lindy S. Statin use is associated with fewer periodontal lesions: A retrospective study. BMC Oral Health 2008; 8:16 (IVSL)
7. Smidt D, Torpet LA, Nauntofte B, Heegaard KM, Pedersen AML. Associations between labial and whole salivary flow rates, systemic diseases and medications in a sample of older people. Community Dent Oral Epidemiol 2010; 38: 422–35.

8. Booth J. A short history of blood pressure measurement. Proceedings of the Royal Society of Medicine 1977; 70 (11): 793–9.
9. Loe H, Silness J. Periodontal disease in pregnancy. I. Prevalence and severity. Acta Odontol Scand 1963; 21: 533-51.
10. Klein H, Palmer CE, Knutson JW. Studies on dental caries: Dental status and dental needs of elementary school children. Public Health Reporter 1938; 53: 751-65.
11. Navazesh M. Methods for collecting saliva. Ann N Y Acad Sci1993; 694: 72-7.
12. Kagawa R, Ikebe K, Enoki K, Murai S, Okada T, Matsuda K, Maeda Y. Influence of hypertension on pH of saliva in older adults. Oral Dis 2013; 19(5): 525-9.
13. Skoglund PH, Svensson P, Asp J, Dahlöf B, Kjeldsen SE, Jamerson KA, Weber MA, Jia Y, Zappe DH, Östergren J. Amlodipine + Benazepril is superior to Hydrochlorothiazide + Benazepril Irrespective of baseline pulse pressure: Subanalysis of the ACCOMPLISH Trial. J Clin Hypertension 2015; 17: 141-6.
14. Cohen M, Khalaila R. Saliva pH as a biomarker of exam stress and a predictor of exam performance. J Psychosom Res 2014; 77(5): 420-5.
15. Nederfors T, Dahlöf C, Twetman S. Effects of the beta-adrenoceptorantagonists atenolol and propranolol on human unstimulated whole saliva flow rate and protein composition. J Dent Res 1994; 102(4): 235-7.
16. Karanxha L, Park SJ, Son WJ, Nör JE, Min KS. Combined effects of simvastatin and enamel matrix derivative on odontoblastic differentiation of human dental pulp cells. J Endod 2013; 39(1):76-82. (IVSL)
17. Landmesser U, Bahlmann F, Mueller M, Spiekermann S, Kirchhoff N, Schulz S, et al. Simvastatin versus ezetimibe: Pleiotropic and lipid lowering effects on endothelial function in humans. Circulation 2005; 111: 2356–63.
18. Maeda T, Matsunuma A, Kurahashi I, Yanagawa T, Yoshida H, Horiuchi N. Induction of osteoblast differentiation indices by statins in MC3T3-E1 cells. J Cell Biochem 2004; 92: 458–71.