Original Article

Effects of Antihypertensive Drugs on Alveolar Bone Loss in Patients with Chronic Periodontitis: A Retrospective Study

AL-Bayaty, F. H.[*,1], Omar Emad Ibrahim[2], William, C.[3], Khairuddin, N. A.[3],

[1] *Center of Periodontology Studies, Faculty of Dentistry, Universiti Teknologi MARA, Sungai Buloh Campus, Jalan Hospital, 47000 Sungai Buloh, Selangor, Malaysia.*

[2] *Center of Preclinical Science Studies, Faculty of Dentistry, Universiti Teknologi MARA, Sungai Buloh Campus, Jalan Hospital, 47000 Sungai Buloh, Selangor, Malaysia.*

[3] *Faculty of Dentistry, Universiti Teknologi MARA, Sungai Buloh Campus, Jalan Hospital, 47000 Sungai Buloh, Selangor, Malaysia.*

Abstract

Objective: This retrospective study aims to evaluate the possible effects of antihypertensive drugs on alveolar bone loss in patients with chronic periodontitis.

Methods: 50 patients on antihypertensive drugs selected as the experimental group and 50 patients with chronic periodontitis with no known systemic illnesses as control group were randomly selected as the study samples. Orthopantomographs were obtained, calibration and assessment of alveolar bone loss was performed by using the computer software program available in the faculty, through radiographic linear measurement procedure. Premolars, first and second molars of both maxilla and mandible were measured from the most apical point to the cementoenamel junction for mesial and distal aspects in the form of millimetres and percentile of the root length. Data was statistically analyzed using independent t-test and Analysis of Covariance in SPSS Version 23 with significance at P-value, $p<0.05$.

Results: A total of 2428 sites were measured. Analysis has shown that there is significant difference in alveolar bone loss in experimental group and control group ($p=0.002$). Bone loss in the experimental group was less (16.28 ± 9.48) compared to the control group (22.66 ± 12.58). Within the experimental group, there was no significant difference for the duration of antihypertensive drug intake. However, the bone loss was more among the males (19.71 ± 11.22) than the females (12.99 ± 5.99).

Conclusion: Antihypertensive drugs appear to have a positive effect on alveolar bone loss progression. Patients under these drugs exhibit lower levels of bone loss compared to those who are not.

Keywords*:* Alveolar bone loss, Antihypertensive drugs, Chronic periodontitis.

Introduction

Chronic periodontitis is defined as inflammation of the gingiva extending into the adjacent attachment apparatus. The disease is characterized by loss of clinical attachment due to destruction of the periodontal ligament and loss of the adjacent supporting bone (1,2). This can ultimately lead to tooth mobility and loss. It can occur in any age with adults and elderly being the most commonly affected (3.) This disease is classified according to

*Corresponding to: AL-Bayaty, F. H., Center of periodontology Studies, Faculty of Dentistry, Universiti Teknologi MARA, Sungai Buloh Campus, Jalan Hospital, 47000 Sungai Buloh, Selangor, Malaysia.

Email: fouad@uitm.edu.my

Tel: +603 61266445

its (1) severity which are mild, moderate and severe, that is determined by the clinical attachment loss, which is the sum of periodontal probing depths and gingival recession, and (2) extent of the disease which are localized, involving less than 50% of the entire dentition, or generalized, involving more than 50% of the entire dentition. The main clinical features of chronic periodontitis are marked inflammatory signs of the periodontium such as edema, bleeding of the gingiva upon probing and this usually results in formation of periodontal pocket and clinical attachment loss and alveolar bone loss (4). The loss of periodontal support can be assessed clinically by assessing the attachment loss and radiographically, the bone levels, with the aid of either periapical radiographs (PA) or orthopantomographs (OPG) (5,6,7).

There are a number of systemic conditions that act as modifying factors, factors that could worsen the condition of this periodontal disease, which have been documented over the years, such as diabetes mellitus, pregnancy, drug-induced disorders, hematological disorders and immune system disorders (8.9). Hypertension is one of the main causes of cardiovascular disease and is the most prevalent chronic disease found among the Malaysian population where the increase in prevalence is directly proportional with age; from 6.7% among the age groups of 18-19 years and up to 75.4% among the age groups 70-74 years. Based on the National Health and Morbidity Survey 2015 carried out by the Ministry of Health, Malaysia, 81.2% of the survey group with known hypertension claimed to be under oral antihypertensive medications (10). There has been evidence showing that antihypertensive drugs can affect the periodontal tissues (11).

Antihypertensive drugs are available anywhere in the market and medical care centers today and they are divided into classes which are, diuretics, beta-blockers, angiotensin-converting enzyme (ACE) inhibitors, calcium channel blockers, alpha-blockers, angiotensin II receptor blockers, alpha II receptor agonists, combined alpha and beta-blockers, central agonists, peripheral adrenergic inhibitors and lastly and vasodilators (12).

It was traditionally thought that thiazide diuretics were able to increase the reabsorption of calcium in the kidneys and thus, increasing the bone mineral density (BMD) and reducing the incidence of bone fractures (13). They were also proven to have a direct stimulation on osteoblast-like cells which results in bone formation (14). These beneficial outcomes were proven in a meta-analysis carried out in 1995 which documented that thiazide diuretics significantly reduces fracture incidence (15). Another class of antihypertensive drugs, the beta-blockers, were also proven to have similar effects such as thiazide diuretics, especially when giving off a protective effect against fracture risks, although limited to only the hip region.[16] A recent study conducted in 2014 also stated that the long-term use of beta-blockers presented a higher BMD in maxilla of patients at high-risk of developing osteoporosis, compared to patients taking calcium-channel blockers, which was actually shown to reduce the BMD instead (17).

It is clear that certain antihypertensive drug classes have an effect on bones (15,17). However, what previous studies have documented, mostly only focused on fracture risks and the effects of these antihypertensive drugs on other bone regions. Through this retrospective study, we aim to investigate the possible effects

of antihypertensive drugs on alveolar bone loss due to the destructive nature of chronic periodontitis.

Materials and Methods

This study was conducted at the Faculty of Dentistry, Universiti Teknologi MARA (UiTM), Sg. Buloh, Selangor, Malaysia. Ethics approval from the UITM research ethics committee was obtained (600-IRMI (5/1/16) REC/186/17, 5 July 2017) to conduct this retrospective study. Samples were taken for this study and they are patients of UiTM Dental Faculty, 43542 folders were analyzed through archive searches, 831 patients were diagnosed with chronic periodontitis had sought for treatment and 42711 non periodontitis. Out of the periodontitis patients143 hypertensive and taking medication (Experimental group) and 688 with no known systemic illnesses (Control) .

Patients who are diagnosed with chronic periodontitis and are taking antihypertensive drugs are categorized into experimental group while those who are having the same periodontal condition with no known systemic illnesses and are not taking any forms of medication are categorized into control group. Patients' records from year 2006 to 2016 were thoroughly went through and obtained from the faculty's existing archive to identify samples that are eligible to be selected according to the inclusion criteria.

Exclusion and inclusion criteria: Patients selection were consenting adults aged ≥ 30 years, of both sex, patients diagnosed with chronic periodontitis and hypertension were on antihypertensive drugs (test group), and patients who were diagnosed with chronic periodontitis with no known medical illnesses (control group). We excluded those with other heart conditions, thyroid diseases, chronic kidney disease, respiratory disorders, rheumatic disorders, diabetes, tobacco users, active orthodontic treatment, wearing removal or fix prosthodontic prosthesis and pregnant women. We also excluded those with less than 50% of their teeth.

Sample size was calculated using Power and Sample Size Calculator version 3.1.2 software program. 50 patients were randomly selected for both experimental and control groups from the archive as the study samples.

Orthopantomographs (OPGs) of the patients were used to assess the average alveolar bone loss (ABL) by using the computer software program (Planmeca Romexis version 2.9.2 software-Finland) available in the faculty through radiographic linear measurement procedure. The inclusion criteria for the selection of OPGs are with (1) high quality (2) adequate brightness and contrast (3) clearly shown anatomical landmarks used in assessing bone loss which includes the cementoenamel junction (CEJ), alveolar crest and bony defects. Inter-examiner, intra-examiner and training calibration session on 5 different OPGs was performed beforehand to evaluate and adjust the precision and accuracy of the measurement equipment. The performance of the examiner was tested by Intraclass Correlation Coefficient (ICC) test. The test was performed using the SPSS version 23 for calibration and value obtained was 0.851, indicating excellent agreement.

Based on the OPGs, all the premolars, first and second molars of both maxilla and mandible were measured from the most apical point to the CEJ for mesial and distal aspects, in the form of millimeters and percentile of the root length. The measurement can only be done on two sites for each tooth as the OPG is a two -dimensional (2D) image. (18,19,20). Measuring a single tooth for both mesial

and distal aspects will give a single ABL value specifically for one tooth. Therefore, the summation of ABL measured for each tooth will give an average ABL for the patient.

$$ABL\,(\%) = \frac{Distance\ between\ CEJ\ and\ the\ alveolar\ bone\ crest}{Distance\ between\ CEJ\ and\ the\ root\ apex} \times 100$$

$$Average\ ABL\,(\%) = \frac{Sum\ of\ ABL}{Number\ of\ sites\ measured} \times 100$$

Data was recorded and statistically analyzed using Independent t-test and Analysis of Covariance (ANCOVA) in SPSS version 23. Independent t-test was performed to interpret the average ABL between the experimental and control groups. ANCOVA is used to control for the effects of extraneous factors that might influence the dependent measure of interest. In our study, this test was done within the same experimental group to evaluate the average ABL in relation with the duration of antihypertensive drug intake, and in relation between genders. The analysis will be elaborated in the results.

Results

Figure 1 shows a total number of 43542 patient folders were examined and only 831 patients were diagnosed with chronic periodontitis. Out of 831 patients, 143 patients have hypertension. However, after taking into consideration the inclusion criteria, only 50 patients were included in this research. 50 patients with chronic periodontitis and no known medical illnesses were randomly selected as the control group. The total number of sites included in the statistical analysis was 2428, with 1142 sites from the experimental group and 1286 sites from the control group.

Table 1 represents the statistical analysis results by using Independent t-test and Analysis of Covariance (ANCOVA) test showed a significant difference of alveolar bone loss in chronic periodontitis patients taking antihypertensive drugs and patients that are not under any form of medication. However, the ANCOVA test showed a more accurate results with a P-value of p=0.002. Horizontal bone loss in the experimental group was less (16.28 ± 9.48) compared to the control group (22.66 ± 12.58).

Table 2 represents the relation between the average alveolar bone loss and the duration of drug-use within the experimental group obtained by the one-way Analysis of Variance (ANOVA) and ANCOVA statistical analysis. It was found that there was no statistically significant difference for both tests between the duration of antihypertensive drug intake among the hypertensive patients (p=0.827, p=0.73).

Table 3 represents the relation between the average alveolar bone loss and the genders within the experimental group. There was a statistically significant difference between male and female within the experimental group based on results obtained from the ANCOVA test (p=0.018). It was found that the horizontal bone loss was more among the males (19.71 ± 11.22) than the females (12.99 ± 5.99).

Discussion

Although chronic periodontitis is the most common form of destructive periodontal disease in adults, it can occur over a wide range of ages. It can occur in both the

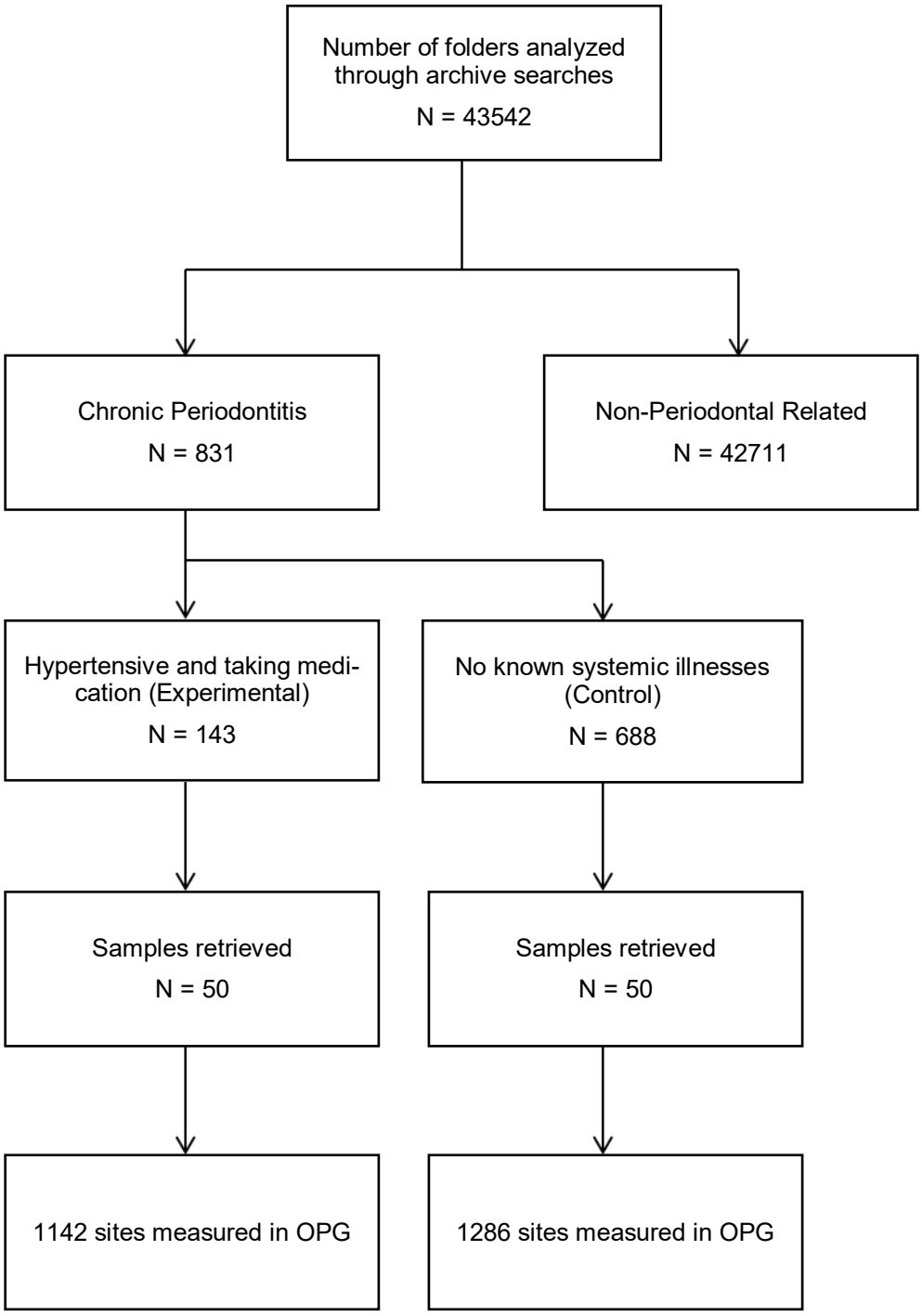

Figure 1: Schematic diagram of search and retrieval of samples

Group	n	Mean	Mean difference (95% CI)	p-value
Experimental	50	[a]16.28 (9.48)	6.38 (1.99, 10.77)	0.005[b]
Control	50	[a]22.66 (12.58)		
Experimental	50	14.95 (11.48, 18.42)	8.04 (-12.94, -3.14)[c]	0.002[d]
Control	50	22.99 (19.53, 26.45)		

[a] Mean (standard deviation)
[b] Independent t-test applied
[c] Adjusted mean difference (95% confidence interval) with Bonferroni adjustment
[d] ANCOVA applied (adjusted for age)
Overall assumptions were fulfilled.

Table 1: Representing the Comparison of Average Alveolar Bone Loss between the Experimental and Control Group

Duration	n	Mean	p-value
0 – 5 years	20	[a]15.89 (9.11)	0.827[b]
6 – 10 years	9	[a]13.67 (10.54)	
More than 10 years	11	[a]15.58 (7.72)	
0 – 5 years	20	16.13 (12.03, 20.24)	0.73[c]
6 – 10 years	9	13.24 (7.11, 19.36)	
More than 10 years	11	15.48 (9.97, 20.99)	

[a] Mean (standard deviation)
[b] One-way ANOVA applied
[c] ANCOVA applied (adjusted for age)

Table 2: Representing the Relation between Average Alveolar Bone Loss and Duration of Drug-Use in the Experimental Group

Gender	n	Mean	Mean difference (95% CI)	p-value
Male	25	[a]19.71 (11.22)	6.72 (1.58, 11.85)	0.012[b]
Female	25	[a]12.99 (5.99)		
Male	25	19.07 (15.51, 22.63)	6.03 (1.09, 10.97)[c]	0.018[d]
Female	25	13.04 (9.62, 16.46)		

[a] Mean (standard deviation)
[b] Independent t-test applied
[c] Adjusted mean difference (95% confidence interval) with Bonferroni adjustment
[d] ANCOVA applied (adjusted for age)
Overall assumptions were fulfilled.

Table 3: Representing the Relation between Average Alveolar Bone Loss and Genders within the Experimental Group

primary and secondary dentition (21). It usually has slow to moderate rates of progression, but may have periods of rapid progression (1). Recent studies suggested the possible association between periodontal disease and hypertension (22,23). Hypertension is one of the most prevalent chronic diseases found in Malaysia (8). However, there have not been sufficient evidences on the exact mechanism of the association between chronic periodontitis and hypertension (24,25). Moreover, a previous study has documented that the prevalence of hypertension in patients with chronic periodontitis was 12.2% and there was no relationship between the severity of chronic periodontitis and hypertension (22). A survey carried out by the Ministry of Health, Malaysia, in 2015 documented that 81.2% of the survey group with known hypertension claimed to be under oral antihypertensive therapy (10). To the best of our knowledge, there have been no studies up to date that documents the relationship between antihypertensive drug -intake and alveolar bone loss in chronic periodontitis patients. Since this is a retrospective study, the aim of this study is not to look at the pharmacological mechanism of the antihypertensive drugs, but instead to investigate the possible effects of the drugs on alveolar bone loss in chronic periodontitis patients.

Results have shown that the alveolar bone loss in patients taking antihypertensive drugs were less compared to those who are not. This finding leads us to believe that there might be a protective effect that antihypertensive drugs produces on the alveolar bone, which coincides with the results of previous studies whereby only certain classes of antihypertensive drugs, specifically thiazide diuretics and beta-blockers, have a protective effect on long bones (13,16,17). Moreover, a study carried out on the comparison of anatomy and histological characteristics between hypertensive patients on renin-angiotensin system (RAS) inhibitors and non-hypertensive patients, found that there was no statistically significant difference in alveolar bone structures between the two groups (26). These findings suggest that not all classes of antihypertensive drugs have an effect on bone cells. However, in our study, we were unable to identify which classes of drugs produce these effects as retrieving a complete patient record was one of our limitations.

There is no significant difference in the relationship of alveolar bone loss and the duration of drug-use within the experimental group. This finding did not coincide with the findings obtained by Ağaçayak et al., which reported that the use of antihypertensive drugs for more than 5 years, specifically the beta-blockers class, shows a higher level of bone mineral density (16). Tezal et al. evaluated the relation between bone mineral density and periodontitis in postmenopausal women, they concluded that skeletal bone mineral density is associated with interproximal alveolar bone loss (27). The long-term use of thiazide diuretics for more than 6 years showed a lower risk of bone fractures in the hip region and thiazide diuretics drug-use of more than 10 years has shown to increase the bone mass of women compared to women who had never used thiazide diuretics before, thus reducing the risk of hip fractures (28,29). These results were contradictory to ours due to the fact that our study considered the duration of drug-use of all antihypertensive drug classes.

We have also found that there is significant difference in genders, whereby males demonstrated a higher amount of bone loss compared to females. This result confirms that men are more predisposed to

periodontal disease compared to women, which coincides with previous studies (30,31). Both studies documented that there is a higher prevalence of periodontal disease in men (≈57%) than in women (≈39%). Gender emerges as a complex socioeconomic and behavioral complex factor that certainly affects access to care, treatment choices, and outcomes; therefore, it needs to be appropriately studied and analyzed. However, given all of the above data, the differences in oral hygiene might be a simplistic explanation for the differences in disease presentation between women and men (31). Our findings have shown that even under the influence of antihypertensive drug-use, the amount of bone loss in patients with chronic periodontitis is still higher among men than women. Our study was subjected to several limitations. One of them, as mentioned before, was the obtaining of a complete patient record. We found that not all vital information was recorded in the patients' folders such as, the type of medications taken, the year on which they started on antihypertensive drugs, radiographic records and the smoking status. This study provides a clear comparison of alveolar bone loss in patients with chronic periodontitis who are on antihypertensive drugs and patients without any systemic illnesses. However, it is helpful to identify the specific types of antihypertensive drugs that give rise to these effects and the mechanism of these drugs on bone cells, in future researches. More researches should be done in the hopes of aiding in the management of chronic periodontitis using certain components of antihypertensive drugs, in the future.

Conclusion

Antihypertensive drugs appear to have a positive effect on alveolar bone loss progression. Patients under these drugs exhibit lower levels of bone loss compared to those who are not. There is no effect on alveolar bone loss in relation to the duration of any antihypertensive drugs intake. Men exhibited a higher amount of bone loss compared to women even under the influence of antihypertensive drug-use.

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