Combined Effect of Systemic Bisphosphonates, Calcium and Vitamin D on Alveolar bone in Osteoporotic Postmenopausal Females having Chronic Periodontitis Following Surgical Periodontal Therapy

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Abstract: This study was conducted to evaluate the systemic use of Alendronate (ALN), an aminobisphosphonate in combination with calcium and vitamin D supplementations on the alveolar bone in osteoporotic postmenopausal females following surgical periodontal treatment of chronic periodontitis. **Subjects and Methods**: Forty postmenopausal osteoporotic females having chronic periodontitis were divided into two groups. Group (1) which is the control group (n=20) received systemic ALN for 6 months. To group (2) which is the study group (n=20) systemic ALN was given in combination with calcium and vitamin D for 6 months. Initial therapy including scaling, root planning and oral hygiene instructions followed by surgical periodontal therapy using the modified Widman flap procedures was performed. The pocket depth (PD) and clinical attachment level (CAL) in addition to radiographic linear, density and angular defect measurements were done at baseline before starting the initial therapy and at 6 months postoperatively. The results revealed a significant gain in clinical attachment level and reduction of pocket depth in both groups with presence of a significant improvement of all the radiographic measurements at the end of the study period. The study group always showed higher percentages of improvement than the control group in all the measurements. It can be concluded that systemic ALN in combination with calcium and vitamin D administration to postmenopausal osteoporotic females is a valuable treatment modality in adjunct to surgical therapy in the management of chronic periodontitis.
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1 Introduction

Osteopenia and Osteoporosis are systemic skeletal disorders characterized by compromised bone strength and mass, with a consequent increase in bone fragility and susceptibility to fracture. Osteopenia is associated with reduction in the amount of bone in addition to the presence of microarchitectural changes without the occurrence of clinical fracture. Osteoporosis on the other hand is associated with high incidence of clinical fracture. It is characterized by reduction in bone mineral density to below the minimum level required to ensure sufficient mechanical support. There is also deterioration of bone tissues due to imbalance between bone resorption and formation, favoring resorption (Koduganti *et al.,* 2009 and Passos *et al.,* 2010).

According to the general diagnostic criteria proposed by the World Health Organization (WHO) and the modification of the International Osteoporosis Foundation, osteoporosis is considered to be present when the bone mineral density (BMD) is 2.5 Standard Deviation (SD) below the average peak bone density achieved in young adults, matched by gender and race. While osteopenia is defined as bone mineral density between one and 2.5 SD below normal BMD level (Wende, 2001 and Shum *et al.,* 2010).

Osteoporosis occurs mainly in postmenopausal females; although younger women and men can be also affected. It was estimated that one in four women during menopause and one in three women > 65 years of age are affected by osteoporosis (Passos *et al.,* 2010).

Postmenopausal osteoporosis in females is characterized by progressive loss of bone tissue that begins after natural or surgical menopause leading to fracture within 15–20 years from the cessation of the ovarian function. The loss of the ovarian function seen in postmenopausal women is accompanied by significant overall changes in skeletal homeostasis (Robet and Louis, 2000 and Kanis *et al.,* 2008).

With regard to periodontal disease, it has been shown that its worldwide prevalence is

10% to 15%, although it may reach 80% in certain regions. Periodontal disease is considered to be the greatest cause of tooth loss and edentulism among adults. The impact of periodontal disease on affected individuals is increasingly apparent and significant with the disease progression, from gingival recession at a relatively early stage with dentin hypersensitivity, toward tooth mobility and pathologic migration leading eventually to tooth loss, thereby affecting chewing and speech functions, esthetics, psychological aspects, and the overall quality of life (Shum *et al.,* 2010).

The evaluation of the relationship between osteoporosis and periodontitis is complicated by the fact that both diseases are multifactorial in the etiology. Multiple systemic factors influence the progression of osteoporosis, including age, race, diet, gender, hormone therapy, smoking, genetic factors, exercise, and body weight. Several of these factors are also risk factors for periodontal disease (Al Habashneh *et al.,* 2010).

It was proven that the periodontal destruction could be significantly influenced by the systemic loss of bone accompanying osteoporosis (Shum *et al.,* 2010). It was also reported that postmenopausal women with osteoporosis and periodontitis are extremely susceptible yielding an excessive response to dental plaque and calculus, as shown by greater bleeding on probing, dentoalveolar bone loss, and decreased alveolar bone mineral density (Passos *et al.,* 2010).

Although periodontal diseases are initiated mainly by bacteria that colonize the tooth surface and gingival sulcus, the host response is believed to play an essential role in the breakdown of connective tissue and bone which are key features of the disease process (Graves *et al.,* 2008).

Periodontal therapy generally consists of mechanical and surgical procedures including the treatment with antibiotics and non steroidal anti-inflammatory drugs (NSAIDS) in some forms of the disease (Rocha *et al.,* 2004). There are data from studies in animals and human trials indicating that pharmacologic agents that modulate the host response believed to be involved in the pathogenesis of periodontal destruction may be effective in slowing the disease progression (Pradeep and Sharma, 2012).

Among these agents, bisphosphonates which are chemical analogs of pyrophosphate; product of human metabolism were found capable of modulating bone mineralization by inhibition of osteoclastic bone resorption. They also have shown osteostimulative properties *in vivo* and *in vitro*, as evidenced by the increase in matrix formation. It was documented that the systemic use of these drugs in postmenopausal women having osteoporosis brings about significant improvement in bone density, resulting in reduced incidence of hip, vertebral, and forearm fractures (Rocha *et al.,* 2004). These agents have been tested in several animal studies and found also effective in treating periodontitis (Jeffcoat *et al.,* 2005).

Alendronate (ALN), an aminobisphosphonate is one of the second generation of bisphosphonates, which was found to be a potent inhibitor of bone resorption. Various studies proved that the systemic use of ALN in humans and some animal models decreased bone loss and increased bone density (Pradeep and Sharma, 2012).

Some anthropological records revealed that humans are exposed to considerably less ultraviolet radiation (required for the synthesis of vitamin D) and consume considerably less calcium than did the early ancestors (Hildebolt, 2005). If calcium intakes are not at or above threshold values, skeletal calcium is resorbed to maintain the body's calcium homeostasis. Dietry calcium intake is important for acieving peak bone mass and maintaining bone density. Dietry intake of vitamin D is essential for calcium absorption. Chronically low intake of calcium and vitamin D can lead to a negative calcium balance, thus causing a secondary increase in calcium removal from bone, including the alveolar bone. Such bone loss may contribute to weakening of the tooth-attachment apparatus (Nishida *et al.,* 2000 and Hildebolt, 2005).

The Food and Nutrition Board (FNB) of the Institute of Medicine has published the well-known recommended dietary allowances (RDA). The adequate intake (AI) that sustains normal health of 1,200 mg/day of calcium and 10.0 g (400 IU)/day of vitamin D for ages 50 to 70 was set (Hildebolt, 2005).

There is evidence that there are possibilities for the management of periodontitis by controlling the systemic risk factors. These observations hypothesize that the combined use of bisphosphonates to regulate skeletal and alveolar bone density with adequate levels of calcium and vitamin D to manage alveolar bone loss associated with periodontal infection is recommended (Nishida *et al.,* 2000, Hildebolt, 2005 and Miley *et al.,* 2009).

The aim of this study is to evaluate the effect of systemic bisphosphonates alone and in

combination with calcium and vitamin D on the alveolar bone in osteoporotic postmenopausal females having chronic periodontitis following surgical periodontal therapy.

2 Subjects and Methods

Study Design

The research was conducted on a selected group of postmenopausal women (≥ 50 years of age) who attended the outpatient clinic in the medical unit of the National Research Center (NRC), Cairo, Egypt for bone densitometry testing in the routine yearly check up. Only women who experienced natural menopause (no menstruation for at least one year) were chosen and invited to participate in this study. They received systemic bone mineral density (BMD) assessment as an initial screening using dual-energy x-ray absorptiometry (DXA) of the hip (Norland XR46 version 3.9.6).

Systemic BMD was classified according to the WHO criteria, where osteoporosis was defined as BMD ≥ 2.5 SDs below the optimal mean BMD of young healthy individuals of the same race and gender. Only postmenopausal females with BMD T-score less than -2.5 SD, where T-score is the expression of BMD values in terms of standard deviations from the normal value of a female young adult mean were included in this study. Women with a history of a systemic condition or medication intake that might influence the BMD or periodontal disease severity were excluded (i.e., women with a history of diabetes mellitus, thyroid diseases, chronic renal problems, and connective tissue diseases). Postmenopausal females on corticosteroids, chemotherapy, recent peptic or esophageal disorders were also excluded. Exclusion criteria also included postmenopausal females treated with drugs that inhibit gastric acid secretion for more than 2 weeks in the last 6 months; chronic treatment with NSAIDs, hormone replacement therapy or any other drug known to alter bone calcium metabolism were not included. Smoking females were not allowed to participate in the study. All patients were systemically reviewed. The participants were chosen to be of the same socio-economic level.

The postmenopausal osteoporotic females who accepted the participation in the study were then referred to the dental clinic at the NRC medical services unit and to the dental clinic at the Faculty of Oral and Dental Medicine, Department of Oral Medicine and Periodontology, Cairo University after making prior appointments for evaluation of their oral condition. All participants received further information about the study protocol and objectives at the dental clinics.

Participants diagnosed as having chronic periodontitis according to the criteria of the American Academy of Periodontology (2000) were chosen. Each patient presented with probing depth (PD) ≥ 5 mm in at least three teeth or periodontal attachment level (PAL) ≥ 4 to 6 mm and vertical bone loss ≥ 3 mm with no history of periodontal therapy or use of antibiotics in the preceding 6 months was selected to be part of the study.

The study included forty non-smoking females, 50-65 years old, who were at least one year postmenopausal, osteoporotic and have not undergone hysterectomy or ovariectomy. All patients were also diagnosed as having chronic periodontitis. Subjects were age-matched into 2 groups of 20 patients each;

Group (1) which is considered the control group included 20 osteoporotic postmenopausal females diagnosed as having chronic periodontitis. The patients in this group received systemic ALN 70 mg/week for 6 months for the treatment of osteoporosis as described in accordance with their physician. In conjunction conventional scaling and root planning followed by surgical periodontal therapy using the modified Widman flap (MWF) procedures as described by Ramfjord and Nissle, 1974 was done.

Group (2) which is considered the study group included 20 osteoporotic postmenopausal females also diagnosed as having chronic periodontitis. This group served as the study group which received ALN 70 mg/week in addition to 1000 mgms of calcium and 400 IU of vitamin D for 6 months. This group was also treated with conventional scaling and root planning followed by surgical periodontal therapy using the same modified Widman flap (MWF) procedures as in group (1).

For both groups detailed oral hygiene instructions were given and full mouth scaling and root planning using ultrasonic scalers and periodontal curettes under local anesthesia was completed before the surgical intervention. Scaling and root planning was performed for each patient in two sessions, one session for each half and completed over one week. Occlusal adjustment was done whenever indicated. Four weeks after the initial therapy the sites that presented pocket depth ≥ 5 mm were allocated to surgical treatment using MWF. Following the surgery sutures were removed after 7 days and

the teeth were polished. Post surgical care included patient's instruction to use 0.12% chlorhexidine gluconate twice daily for assisting plaque control for 7 days. Neither brushing nor manipulation of the surgical site is attempted for 10 days. Patients were seen every 3 weeks for 6 months at which time the teeth were polished and the oral hygiene instructions were reviewed. The participating women were informed about the nature, objectives, and possible risks of the study, and they signed informed consent statement that authorized their inclusion in the study.

Clinical Study

Women in both groups received ALN. They were given blister packs of pills containing 70 mg ALN. They were instructed to take one tablet of ALN in the morning, at least 30 minutes before breakfast or at least 2 hours after breakfast once weekly. Patients in group (2) were instructed to take 70 mg/week ALN in addition to 1000 mgms calcium and 400 IU vitamin D/ daily. Patients were followed up every 2 weeks for 6 months. Medication compliance was assessed at each visit by counting the tablets remaining in the blister packs. During each visit, bacterial plaque (BP) was assessed using plaque detection tablets and flossing technique was reviewed. During the study period, all patients within the same group received identical periodontal assessment and treatment.

Periodontal Assessment

Periodontal assessment was carried out at baseline before starting the initial therapy and the surgical procedures and at the end of the study (6 months postoperatively). At the baseline evaluation, all clinical parameters were measured and mechanical treatment including removal of all supra and subgingival calcified deposits to obtain a smooth, hard surface was done. Scaling and root planning was carried out by one of the investigators in two successive sessions. Patients were taught and encouraged to maintain their dental health and plaque control through brushing and flossing. All assessment measurements were taken by the same investigator. The condition of all teeth was assessed and recorded. The mean was taken for the following measurements: whole mouth probing depth and clinical attachment level.

Pocket depth (PD) was measured according to the standard procedure described by Glavind and Loe, 1967 using a periodontal probe with Williams' calibrations at the free gingival margin and recorded at six locations (mesiobuccal, distobuccal, midbuccal, mesiolingual, distolingual and midlingual) on each tooth parallel to the long axis of the examined tooth. The total of the mean probing depth at the six locations on each tooth for each patient was calculated in millimeters. The distance from the cemento-enamel junction (CEJ) to the free gingival margin and the distance from the free gingival margin to the bottom of the pocket/sulcus (PD) were measured at the mesio-buccal and mid-buccal surfaces using also a calibrated probe. From these two measurements, individual subject mean attachment level (the distance from the CEJ to the bottom of the pocket or sulcus) was calculated in millimeters. All the measurements were taken at baseline and 6 months.

Radiographic parameters:

Bone mineral density (BMD) was measured for each patient by Dual-energy X-ray absorptiometry (DXA) of the hip using Norland XR46 version 3.9.6 for diagnosis of osteoporosis. Standardized intraoral periapical radiographs using the paralleling technique were taken at baseline and 6 months post-operatively using Trophy x-ray machine with exposure parameters of 60 KVP, 10 mA and 0.14 sec (Trophy radiology, 94300 Vincennes, type 6510, made in France). The paralleling technique was used with Rinn XCP film holder (KKD Germany), which consists of interchangeable acrylic bite blocks, a plastic aiming ring and a metallic indicator arm.

For each patient an occlusal stent was constructed to confirm reproducibility and standardization of the technique. The alveolar bone changes were measured from the radiographs using the measurement system of the Digora software (Orion Corporation, Sordex Medical System, Finland).

1- Linear Measurements calculated in millimeters (mm):

a) A line was drawn from C.E.J to the alveolar crest in each defect parallel to the long axis of the studied tooth at the most radiographically accentuated point (A).

b) Another line was drawn from the alveolar crest to the apex to the long axis of each studied tooth (B).

The same investigator performed the measurements twice and the mean of both trials was calculated as an attempt to eliminate intra-observer errors.

2- Densitometric Measurements (gram / cubic centimeter):

For performing standardized densitometric analysis, 3 successive straight lines were drawn each 1 mm apart and parallel to each other and to the root surface reaching the most radiographically accentuated points.

a) The first line was drawn from C.E.J to the alveolar crest in each defect parallel to the long axis of the studied tooth (A).

b) The second line was drawn from the alveolar crest to the apex to the long axis of each studied tooth (B).

c) The third line was drawn from C.E.J to the apex parallel to the long axis of each studied tooth (C). The mean value of each line was measured and their means were calculated.

The same investigator performed all the measurements for each line twice and the mean of the trials was calculated as an attempt to eliminate intra-observer errors.

3- Radiographic defect angle measurements (degree):

The radiographic defect angle was calculated and defined by two lines that represented the root surface and the bone-defect surface. The defect angle is the angle between the two lines one drawn from CEJ to the bone defect and the other one is drawn from the bone defect to the alveolar bone crest at the most radiographically accentuated point (Fernanda *et al.*, 2011).

Statistical Analysis

Descriptive statistics including the mean and standard deviation were calculated. Also the *P* value was measured. The Wilcoxon matched pairs test was used to compare pre and post treatment values. The Mann-Whitney test was used to compare between the two groups. The significant level was set at $P \leq 0.05$ (Dawson and Trapp 2001). Statistical analysis was performed with SPSS 16.0 (Statistical Package for Scientific Studies) for Windows (SPSS, Inc., Chicago, IL, USA).

3. Results

A) Clinical assessment:

1- Probing depth (PD) measurements:

Comparison of the mean PD values of the control and study groups at baseline and six months postoperatively revealed that there was no statistically significant difference between the two groups before treatment. After surgical treatment with MWF, the study group showed more statistically significant reduction of the PD as compared to the control group as presented in table (1).

Table (1) shows the mean ± SD, percentages of change and *P* values of PD measurements of both control and study groups at baseline and six months postoperatively. Significance was set at $P \leq 0.05$.

Group	Control group	Study Group	
Treatment	Mean ± SD	Mean ± SD	*P*-value
Baseline	6.66 ± 1.4	6.69 ± 1.3	0.388
Six months	5.12 ± 1.4	4.48 ± 1.1	0.354
Mean Difference	1.54	2.21	0.001
% of PD reduction	23.12%	33.03%	

2- Clinical attachment level (CAL) measurements:

Comparison of the mean CAL values of the control and study groups at baseline and six months postoperatively revealed that there was no statistically significant difference between the two groups before treatment. After surgical treatment with MWF, the study group showed more statistically significant gain of the clinical attachment after six months as compared to the control group as shown in table (2).

Table (2) shows the mean ± SD, percentages of change and P values of CAL measurements of both control and study groups at baseline and six months postoperatively. Significance was set at $P \leq 0.05$.

Group	Control group	Study Group	
Treatment	Mean ± SD	Mean ± SD	*P*-value
Baseline	5.66 ± 1.2	5.66 ± 0.9	0.154
Six months	4.55 ± 1	4.35 ± 0.8	0.717
Mean Difference	1.11	1.31	0.001
% of CAL gain	19.61 %	23.14%	

B) Radiographic assessment:

1) Linear measurements of the control group:

Table (3) demonstrates the linear measurements (A) and (B) pre and post treatment for the control group. There was a significant difference in the Wilcoxon matched pairs test between pre and post treatment values with a *P*-value of (0.0001) for both measurements.

Table (3) is showing the mean ± SD, percentages of improvement and *P* values of linear measurements (A) and (B) pre and post treatment for the control group.
SD: standard deviation, *P*: probability, I: improvement, S: significance or significant, NS: non-significant.

Control group	Linear measurement (A)		Linear Measurement (B)	
	Baseline	Six months	Baseline	Six months
Mean±SD	6.49 ±1.41	5.6 ±1.42	12.37 ±2.28	13.08±2.33
P-value	0.0001		0.0001	
S	S		S	
% of improvement	13.55%		5.73%	

2) Linear measurements of the study group:

Table (4) shows the linear measurement (A) and (B) pre and post treatment for the study group. There was a significant difference in the Wilcoxon matched pairs test between pre and post treatment values with a *P*-value of (0.0001) for both measurements.

Table (4) Showing Mean ± SD, percentages of improvement and P values of linear measurements (A) and (B) pre and post treatment of the study group.

Study group	Linear measurement (A)		Linear measurement (B)	
	Baseline	Six months	Baseline	Six months
Mean ±SD	6.32 ±1.32	4.48 ±1.11	12.92 ±1.99	15.63 ± 1.83
P-value	0.0001		0.0001	
S	S		S	
% of I	23.41 %		20.97 %	

3) Comparison between control and study groups in the linear measurements:

Table (5) revealed the Mann-Whitney test results for the linear measurements (A) and (B) pre and post treatment between control and study groups. There was no significant difference in pre treatment values as the *p*-value was (0.54), while there was a significant difference in the post treatment values where *p*-value was (0.02) in measurement (A). While for measurement (B) there was also no significant difference in pre treatment values as the *p*-value was (0.39), while there was a significant difference in the post treatment values where *p*-value was (0.0001).

Table (5) Showing Mann-Whitney test results between control and study groups for linear measurements (A) and (B) pre and post treatment.

Mann Whitney test	Linear measurement (A)		Linear measurement (B)	
	Baseline	Six months	Baseline	Six months
Mann Whitney U value	281.0	195.5	269.0	113.0
P-value	0.54	0.02	0.39	0.0001
S	NS	S	NS	S

4) Density measurements of the control group:

Table (6) demonstrates the density measurements (A), (B) and (C) pre and post treatment of the control group. There was a significant difference in the Wilcoxon matched pairs test between pre and post treatment values as *P*-value was (0.001) for the (A) measurements. Also for the (B) measurements as *P*-value was (0.002). In addition there was a significant difference in the
Wilcoxon matched pairs test between pre and post treatment values as *P*-value was (0.0001) for the (C) measurements.

Table (6) Showing Mean ± SD, percentages of improvement and *P* values of density measurements (A), (B) and (C) pre and post treatment for the control group.

Control group	Density (A)		Density (B)		Density (C)	
	Baseline	Six months	Baseline	Six months	Baseline	Six months
Mean ±SD	40.5 ±18.05	44.98 ±16.43	128.31 ±13.48	131.28 ±14.37	110.4 ±24.28	115.2 ±21.39
P	0.001		0.002		0.0001	
S	S		S		S	
% of I	11.03%		2.31%		4.34%	

5- Density Measurements for the study group:

Table (7) demonstrates the density measurements (A), (B) and (C) pre and post treatment for the study group. There was a significant difference in the Wilcoxon matched pairs test between pre and post treatment values as *P*-value was (0.0001) for all the measurements (A), (B) and (C).

Table (7) Shows Mean ± SD, percentages of improvement and *P* values of density measurements (A), (B) and (C) pre and post treatment for the study group.

Study group	Density (A)		Density (B)		Density (C)	
	Baseline	Six months	Baseline	Six months	Baseline	Six months
Mean ±SD	45.09 ±32.66	65.31 ±36.49	132.0 ±15.01	143.28 ±14.82	111.92 ±15.35	129.88 ±16.55
P-value	0.0001		0.0001		0.0001	
S	S		S		S	
% of I	44.84%		8.53%		16.03%	

6- Comparison between the density measurements in the control and study groups:

Table (8) reveals the Mann-Whitney test results for the density measurements (A), (B) and (C) pre and post treatment between control and study groups. There was no significant difference in pre treatment values while there was a significant

difference in the post treatment values of (A), (B) and (C) measurements.

Table (8) Mann-Whitney tests between control and study groups for density measurements (A), (B) and (C) pre and post treatment.

Mann Whitney test	Density (A)		Density (B)		Density (C)	
	Baseline	Six months	Baseline	Six months	Baseline	Six months
Mann Whitney U value	300.0	202.0	282.0	206.0	284.0	206.5
P-value	0.8	0.03	0.55	0.03	0.55	0.04
S	NS	S	NS	S	NS	S

7- Angle defect measurements

Table (9) demonstrates the defect angles pre and post treatment for control and study groups.

There was a significant difference in the Wilcoxon matched pairs test between pre and post treatment values as *P*-value was (0.02) in the control group and *P*-value was (0.00001) in the study group.

Table (9) shows the Mean ± SD, percentages of improvement and P values of defect angles pre and post treatment for the control and study groups.

Defect angle measurements	Control Group		Study group	
	Baseline	Six months	Baseline	Six months
Mean ±SD	57.0 ±14.12	59.96 ±13.15	55.11 ±13.64	67.72 ±10.87
P-value	0.02		0.0001	
S	S		S	
Percentage of improvement	5.19%		22.88%	

8- Comparison between the defect angle measurements in the Control and Study groups:

Table (10) reveals the Mann-Whitney test results for the defect angles pre and post treatment between control and study groups. There was no significant difference in pre treatment values where the *p*-value was (0.77), while there was a significant difference in the post treatment values where *p*-value was (0.04).

Table (10): shows the Mann-Whitney test of defect angles between control and study groups pre and post treatment.

Mann-Whitney test	Angles	
	Baseline	Six months
Mann-Whitney U value	298.0	207.0
P-value	0.77	0.04
S	NS	S

Table (11) shows percentages of improvement of all the measurements in both groups revealing that in all the clinical and radiographic measurements the study group showed higher percentages of improvement than the control group.

Group	Control group	Study Group
Measurements		
PD	23.12	33.03
CAL	19.61	23.14
Linear (A)	13.55	23.41
Linear (B)	5.73	20.97
Density (A)	11.03	44.84
Density (B)	2.31	8.53
Density (C)	4.34	16.03
Defect angle	5.19	22.8

4. Discussion

Osteoorosis is often called the "silent disease" because bone loss occurs without symptoms. People are not aware that they have osteoporosis until their bones become so weak that a sudden strain, bump or fall causes a fracture or a vertebra to collapse (Ghozlani *et al.,* 2009). Osteoporosis is one of the risk factors that have been implicated in the progression of periodontitis (Graves & Cochran, 2003). A number of studies showed that there is a relationship between oral and systemic bone loss as well as an association of osteoporosis with periodontal diseases (Brennan *et al.,* 2007, Nackaerts *et al.,* 2008 and Shum *et al.,* 2010).

Understanding the association between periodontal disease and osteoporosis and the mechanisms underlying this association may aid health professionals in the prevention, early detection, and treatment of these common diseases (Shum *et al.,* 2010). Bisphosphonates are widely utilized pharmacological agents in the management of systemic metabolic bone diseases (including osteoporosis) due to their ability to inhibit bone resorption. During bone resorption they can be taken up by the osteoclast, resulting in osteoclast de-activation and apoptosis. Various studies have demonstrated that bisphosphonates not only induce the osteoblasts to secrete inhibitors of osteoclast-mediated resorption but also stimulate the formation of osteoblasts precursors and mineralized nodules, thereby promoting early osteoblastogenesis (Rocha *et al.,* 2004). There is also reduction of activity and prevention of the development of osteoclasts from hematopoietic precursors. Bone resorption is suppressed followed by a secondary mineralization resulting in increased bone mass, improving bone strength

and reduction in fractures (Menezes *et al.,* 2005). Bisphosphonates are often considered the first-line therapy for the treatment of post-menopausal osteoporosis. They are the most widely prescribed anti-resorptive agents.

Randomized clinical trials of ALN demonstrated increase in bone mineral density in post-menopausal women with osteopenia or osteoporosis. In women with osteoporosis a reduction in the incidence of hip, vertebral and non-vertebral fractures of nearly 50% were noted (Koduganti *et al.,* 2009). In addition ALN was found capable of preventing periodontal ligament destruction in several experimental periodontitis studies. It was also documented that the systemic administration as well as the local delivery of ALN reduced alveolar bone loss without interfering with bone formation in procedures involving mucoperiosteal flap surgery (Reddy *et al.,* 2005 and Pradeep & Sharma, 2012).

ALN was proven to preserve alveolar bone through its anti-inflammatory and antibacterial activities in experimental periodontitis. ALN is capable of inhibiting the neutrophil influx which has been linked to tissue destruction in a number of inflammatory diseases such as rheumatoid arthritis and periodontitis. ALN is also capable of reducing the mononuclear cell infiltration in gingival tissue. Circulating monocytes may differentiate locally into osteoclasts, thereby exerting bone resorbing activity; this may contribute to the bone sparing effect of ALN. Regarding the antibacterial activity ALN can inhibit the growth of the bacteria characteristic of periodontal disease. It is possible that the antibacterial activity of ALN might result, at least partially, from the prevention of bone destruction and reduction of the periodontal pocket which was noted in the present study as explained by Menezes *et al.,* 2005.

Additionally Rocha *et al.,* 2001 have used systemic ALN for 6 months in the treatment of periodontitis patients with type II diabetes and reported significant improvement in the healing response compared to the placebo group. Another study found significant decrease in clinical parameters such as plaque index; gingival index and PD with significantly gain in CAL. The percentage of bone fill in the ALN group was 40.4 ± 11.71% compared to 2.5 ± 1.02% in the placebo group after 6 months therapy as reported by Rocha *et al.,* 2004. This was in line with the present study in which there was a significant reduction of pocket depth and a significant gain in clinical attachment level in both control and study group. Also the radiographically measured parameters should a significant improvement at the end of the 6 months treatment period.

The improvement noted in the present study can be contributed to the combined mechanical treatment, and the oral hygiene instructions our patients received in addition to the surgical periodontal therapy and the administration of ALN. In this study postmenopausal women were selected because they are at increased risk for bone loss including alveolar bone and are more likely affected by osteoporosis as a result of estrogen deficiency (Haas *et al.,* 2009 and Pradeep & Sharma, 2012).

Females at the postmenopausal period experience diverse physical and emotional symptoms. Change in dietary habits, and oral changes are frequently found among these women. There is also higher prevalence of periodontal disease and osteoporotic jaws (Rocha *et al.,* 2004).

It appears that as people age, they take less dietary calcium and vitamin D possibly because of their decrease of total food intake. They are also less exposed to the sun due to the limitations of their movements. So it is reasonable that they take supplements to fulfill their requirements to prevent bone resorption or future disease as stated by Nishida *et al.,* 2000.

It was proven that elderly women who took calcium and vitamin D supplementation were less likely to be periodontitis cases. Various data suggests that calcium and vitamin D intake by adult periodontal maintenance patients is associated with better periodontal health. It was documented that lower dietary intake of calcium increased the risk of periodontal disease in a dose-response relationship (Al Habashneh *et al.,* 2010).

The National Osteoporosis Foundation as well as the National Academy of Sciences thus recommended a daily intake of 1200 mgms of calcium and 400-600 IU of vitamin D (Koduganti *et al.*,2009). This is why the postmenopausal females in our study group were given calcium and vitamin D supplementations.

To our knowledge the combined use of ALN, calcium and vitamin D and its effect on alveolar bone especially following surgical management of intrabony lesions in chronic periodontitis patients was not investigated. So we hypothesized that this combination will yield better results than using ALN alone. This hypothesis was proven to be correct because all the linear, density and angular defect measurements in addition to the clinical

parameters records (PD and CAL) of our study revealed that the results of the study group were always showing a higher percentage of improvement than the control group. This was in agreement with studies documenting that vitamin D and calcium oral supplementation were effective in improving the periodontal condition and were used as a useful adjunctive treatment. This adjunct treatment was found capable of decreasing the damage (clinical attachment and alveolar crest height loss) caused by periodontal disease .The investigators also suggested that vitamin D may reduce the susceptibility to gingival inflammation through its anti-inflammatory effect. It was also demonstrated in a 3-year study that increased intake levels of calcium and vitamin D had a beneficial effect on tooth retention (Miley *et al.,* 2009) which is in conformity with the present study. This is why clinicians always rely on parameters such as PD reduction, CAL gain and radiographs to evaluate a treatment modality as performed in the current study (Froum *et al.,* 2001).

Many studies where osseous surgery was performed, pocket reduction was greater than with scaling or curettage (Becker *et al.,* 2001). The main advantage of the modified Widman flap surgery done in the current study over any other periodontal surgical procedure is the intimate postoperative adaptation of healthy collagenous tissues to all tooth surfaces. It has been shown experimentally in animals and humans that with a close adaptation of gingival tissues to the tooth surface, a marginal new epithelial attachment forms which tends to seal off the deeper areas of separation between the tooth and the surrounding tissues. Thus the healing connective tissues may adapt as closely to the tooth surfaces as to an implant and reattachment with formation of new cementum may develop gradually from the apical aspects of the lesion. In such cases minimal or no inflammation is present indicating that the pathologic periodontal pocket has been eliminated as a source of irritation (Ramfjord and Nissle, 1974 and Becker *et al.,* 2001).

DXA performed at the start of the study in the diagnosis of osteoporosis is capable of detecting small changes in bone mineral content at multiple anatomic sites with excellent precision (0.5% to 2%) and accuracy (3% to 5%). Assessment of alveolar bone following surgical treatment of intrabony defects was evaluated by a digital imaging system using standardized periapical radiographs. Much diagnostic information is available from digital radiographs which allows for detection of mineral changes as little as 5% (Woolhiser *et al.,* 2005). They are valuable in the detection of early to moderate bone changes, approximating the amount of bone loss and its location, and helping in the prognosis of the affected teeth serving as baseline data and as means of evaluation of post treatment results (Tugnait and Hirschmann, 2003).

Conclusion

The combined use of ALN, calcium and vitamin D showed better improvement in treatment outcomes in both the clinically and radiographically measured parameters proving that this combination is a valuable treatment modality in management of chronic periodontitis in adjunct to the surgical periodontal therapy.

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5. References

Al Habashneh R., Alchalabi H., Khader Y. S., Hazza'a A.M., Odat Z, and Johnson G.K. : Association Between Periodontal Disease and Osteoporosis in Postmenopausal Women in Jordan. J Periodontol., 2010; 81:1613-1621.

American Academy of Periodontology: Parameter on chronic periodontitis. J Periodontol., 2000; 71: 853-855.

Becker W., Becker B.E., Caffesse R., Kerry G., Ochsenbein C., Morrison E. and Prichard J.: A longitudinal study comparing scaling, osseous surgery, and modified Widman procedures: Results after 5 years. J Periodontol., 2001; 72: 1675-1684.

Beitz J and Doren M: Physical activity and postmenopausal health, J Br Menopause Soc., 2004**,** 10: pp. 70–74.

Brennan R. M., Genco R. J., Hovey K. M., Trevisan M. and Jean Wende J.W.: Clinical Attachment Loss, Systemic Bone Density, and Subgingival Calculus in Postmenopausal Women. J Periodontol., 2007; 78:2104-2111.

Dawson B. and Trapp R.G. Basic and Clinical Biostatistics, New York: (2001). Lange Medical Books-McGraw Hill. **Fernanda V. R., Renato C.V. C., Francisco H.N. J., Enilson A. S. and Ma´ rcio Z. C.** The Role of Enamel Matrix Derivative Protein in Minimally Invasive Surgery in Treating Intrabony Defects in Single-Rooted Teeth: A Randomized Clinical Trial. J Periodontol 2011; 82:522-532.

Ghozlani I., Ghazi M., Nouijai A., Mounach A.,

Achemlal R. A., Bezza A. and El Maghraoui A.: Prevalence and risk factors of osteoporosis and vertebral fractures in patients with ankylosing spondylitis. Bone, 2009, 44(5): 772-776.

Glavind L. and Löe H.. Errors in the clinical assessment of periodontal destruction. J Periodont Res., 1967; 2: 180-188.

Graves D.T. and Cochran D.: The contribution of interleukin-1 and tumor necrosis factor to periodontal destruction. J Periodontol., 2003; 74: 391-401.

Graves D. T., Fine D., Teng Y. A., Van Dyke T. E., Hajishengallis G .: The use of rodent models to investigate host–bacteria interactions related to periodontal diseases. J of Clin Periodontolo., 2008; Vol. 35, Issue (2): pp. 89–105.

Froum S.J., Weinberg M.A., Rosenberg E. and Tarnow D.: A comparative study utilizing open flap debridement with and without Enamel Matrix Derivative in the treatment of periodontal intrabony defects: A 12-Month Re-entry study. J Periodontol., 2001; 72:25-43

Haas A.N., Cassiano K., Ro¨sing, Oppermann R. V., Jasim M. Albandar, and Susin C. Association Among Menopause, Hormone Replacement Therapy, and Periodontal Attachment Loss in Southern Brazilian Women. J Periodontol., 2009; 80:1380-1387.

Hildebolt C.F.: Effect of Vitamin D and Calcium on Periodontitis. J Periodontol., 2005; 76:1576-1587**.**

Jeffcoat M.: The Association between Osteoporosis and Oral Bone Loss. J Periodontol., 2005;76 :2125-2132..

Kanis J.A., Burlet N. and Cooper C.: European guidance for the diagnosis and management of osteoporosis in postmenopausal women, Osteoporosis Int. 2008**,** 19: 399–428.

Koduganti R.R., Gorthi C, Reddy P. V., and Sandeep. N. Osteoporosis: "A risk factor for periodontitis". J Indian Soc Periodontol., 2009; 13 (2): 90-96.

Menezes A. M.A., Rocha F.A. C., Chaves H. V., Carvalho C. B.M., Ribeiro R. A. and Brito G. A. C.: Effect of Sodium Alendronate on Alveolar Bone Resorption in Experimental Periodontitis in Rats. J Periodontol., 2005; 76:1901-1909.

Miley D. D., Garcia M. N., Hildebolt C. F., Shannon W. D., Couture R.A., Spearie C. L. A., Dixon D. A., Langenwalter E. M., Mueller C. and Civitelli R.: Cross-Sectional Study of Vitamin D and Calcium Supplementation Effects on Chronic Periodontitis. J Periodontol., 2009; 80:1433-1439.

Nackaerts O., Frieda G., Anna-Maria S. and Reinhilde J.: Is there a relation between local bone quality as assessed on panoramic radiographs and alveolar bone level? Clin Oral Invest.; 2008, 12: 31–35,

Nishida M., Grossi S.G., Dunford R.G., Ho A.W., Trevisan M. and Genco R.J.: Calcium and the risk for periodontal disease. J Periodontol., 2000; 71: 1057-1066.

Passos J. D., Gomes-Filho I. S., Vianna M. I. P., da Cruz S.S., Barreto M. L., Oliveira T. J., Borges L. D., and Monteiroi F.M. Outcome Measurements in Studies on the Association between Osteoporosis and Periodontal Disease. J Periodontol., 2010; 81:1773-1780.

Pradeep A. R. and Sharma A. Clinical Efficacy of 1% Alendronate Gel as Local Drug Delivery System in the Treatment of Chronic Periodontitis - A Randomized Controlled Clinical Trial". J Periodontol., 2012; 83(1):11-8.

Ramfjord S.P. and Nissle R.R. The Modified Widman Flap. J Periodontology, 1974; vol. 45, no. (8): 601-607.

Reddy GT, Kumar PM, Veena KM. Formulation and evaluation of alendronate sodium gel for the treatment of bone resorptive lesions in periodontitis. Drug Delivery, 2005; 12: 217-222.

Robet L. and Louis A.V.: Estrogen and selective estrogen receptor modulators for prevention and treatment of osteoporosis: The osteoporotic syndrome, 2000, 7(5): 101-120.

Rocha M. L., Nava L.E., De La Torre C.V., Sanchez-Martin F., Garay-Sevilla M.E. and Malacara J.M.: Clinical and radiological improvement of periodontal disease in patients with type 2 diabetes mellitus treated with alendronate: A randomized placebo-controlled trial. J Periodontol., 2001; 72: 204-209.

Rocha M. L., Malacara J. M., Sánchez-Marin F. J., de la Torre C.J. V., and Fajardo M. E. Effect of Alendronate on Periodontal Disease in Postmenopausal Women: A Randomized Placebo-Controlled Trial. J Periodontology 2004; 75:1579-1585.

Shum I., Leung P.C., Kwok A., Corbet E. F., Orwoll E. S., Phipps K.R., and Jin L. Periodontal Conditions in Elderly Men with and without Osteoporosis or Osteopenia. J Periodontology, 2010; 81:1396-1402.

Tugnait A.C.V. and Hirschmann P.N.: Radiographic equipment and techniques used in general dental practice: a survey of general dental practitioners in England and Wales, J. Dent. 2003**,** 31: 197–203.

Wende J.W.. Periodontal Diseases and Osteoporosis: Association and Mechanisms. Ann Periodontology, 2001; 6:197-208.

Woolhiser G.A., Brand J.W., Hoen M.M., Geist J.R., Pikula A.A. and Pink F.E.: Accuracy of film-based**,** digital, and enhanced digital images for endodontic length determination. Oral Surg, Oral Med, Oral Path, Oral Radiol Endod.; 2005, 99: 499-504**.**