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Assessment of the effects of Alendronate treatment on clinical periodontal parameters in postmenopausal women with osteoporosis.

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ABSTRACT

Osteoporosis and periodontal disease stand for a major health problem principally in aged women with complex as well as recognized bidirectional association. Postmenopausal osteoporosis also known as type I osteoporosis typifies a common illness in womanly patients by the beginning of menopause, owing to estrogen reduction after menopause. Alendronate is a first line drug for treatment of postmenopausal osteoporosis and it is a powerful inhibitor of osteoclast action that diminish bone resorption moreover, it was suggested of having osteo stimulative property in vivo and in vitro as revealed through increase in bone matrix formation. Thus medical management of postmenopausal osteoporosis women with alendronate may well have valuable outcome on periodontal health condition. 1.To estimate and compare the periodontal health status of the study and control groups. 2. To assess the effect of alendronate treatment on clinical periodontal parameters (plaque index(PLI),gingival index(GI),bleeding on probing(BOP),probing pocket depth(PPD),and clinical attachment level(CAL) in postmenopausal women with osteoporosis.3.To correlate between Alendronate intake duration and clinical periodontal parameters. 90 participants, females only were conscripted in this study with age ranged from (55-65) years old, were divided into three groups, (30 subjects each):first control group systemically healthy with healthy periodontium, second group postmenopausal women with osteoporosis under alendronate treatment for (3-6)months(Alendronate group) ,third group postmenopausal women with osteoporosis only without alendronate treatment(Osteoporosis group), the last two groups were sub divided in to two sub group each one consist of 15 gingivitis and 15 periodontitis . Periodontal health status was determined by clinical periodontal examination of plaque index (PLI), gingival index (GI), bleeding on probing (BOP), probing pocket depth (PPD) and clinical attachment level (CAL). Postmenopausal women with osteoporosis demonstrated the highest median values of all clinical periodontal parameters followed by Alendronate group, then the control group with healthy periodontium and systemically healthy (except for plaque index with higher value in Alendronate group). total correlation between drug intake duration and clinical periodontal parameters were weak negative non significant with (BOP, PPD,CAL) except for(PLI , GI) there were strong positive highly significant and weak positive highly significant correlation respectively between them. Patients with osteoporosis had greater periodontal tissue destruction comparing with patients with alendronate treatment with less periodontal tissue destruction. Additionally alendronate treatment may have beneficial outcome on periodontal health status in postmenopausal women with osteoporosis and periodontal disease.

Keywords: periodontal diseases, Osteoporosis, Alendrona

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INTRODUCTION

Periodontal diseases (PD) are an assortment of inflammatory conditions that influence the supporting tissues of the teeth which include: tissue of gingiva, periodontal ligaments, cementum and alveolar bone [**1].** The two forms of periodontal diseases are gingivitis and periodontitis. Gingivitis means inflammation of the soft tissue of gingiva, which is not extending to the connecting ligaments, while periodontitis involves profounder periodontal tissue leading to detachment of connecting ligaments along with the destruction of gingiva, cementum as well as alveolar bone [**2] ,** periodontal pocket formation, all these symptoms will lead to tooth mobility and finally tooth loss [**3].** Although periodontal diseases are principally occurs as a result of bacteria that fixed to the tooth facade and inhabit gingival cleft, the host response is considered to play a significant function in the damage of connective tissue and bone which are key elements of the disease progression [**4]**. Osteoporosis (OP) and periodontal diseases share identical risk factors. Prevalence of both conditions increase with increasing age in females [**5].** Postmenopausal osteoporosis (PMO) is osteoporosis that take places following menopause due to estrogen reduction [**6].**which lead to prompt bone resorption [**7],** that also involves jawbones [**8,9],** and increase the damage rate of connective tissue of gingiva by stimulating the synthesis of many cytokines responsible for bone resorption[**10].** Many researchers propose that postmenopausal osteoporosis provoke periodontitis [**6].** It has been verified that bacterial products in PD induce alveolar bone resorption by osteoclast through releasing of toxins and inflammatory cytokines [**11],** that also released in postmenopausal osteoporosis [**12].** Alendronate (ALN) considered the first line remedy for the treatment of postmenopausal osteoporosis, as well as it is the most broadly prescribed antiresorptive drugs [**13]**. Clinical experiments confirmed that ALN notably raise bone mineral density at the spine and hip in younger and adult postmenopausal women [**14, 15]**. While periodontal diseases are multifactorial in etiology, different treatment options are concerned [**16]**.Modulation of host through using chemotherapeutics substances is an interesting novel adjunctive curative opportunity for managing PD [**17].** Evidences from animals as well as human trials verified that pharmacological mediators like ALN that adjust destructive feature of host reaction may possibly have advantageous outcome on disease development [**18].**One most important research center on ALN in periodontal therapy is the fortitude of its outcome on bone resorption beside the clinical parameters in experimental animal. [**19,20].**

MATERIALS AND METHODS

Ninety participants were selected to take part in the study, consist of females only with age range between (55-65 years) .Samples collection was started from 7th December 2016 till 2th April 2017. The samples were collected from patients attended to the department of Rheumatology of Baqubah teaching hospital in Baqubah city. Each subject was carefully knowledge concerning the purpose of the study and allowable to its protocol and they were permitted to consent or refuse to be included in the study. Every subject was examined by DEXA scan for diagnosis of Osteoporosis, osteopenia or normal T-score. All subjects divided into three main groups:-

1-First group **(Control group):** Thirty control healthy postmenopausal women (Systemically and periodontally).
2-Second group **(ALN group):** Thirty post postmenopausal osteoporosis women under ALN treatment for 3-6 months divided in to two sub groups **(**15participants of them were gingivitis and 15 chronic periodontitis) **(ALNg, ALNp).**
3-Third group **(OP group):** Thirty post postmenopausal osteoporosis women also divided in to two sub groups (15participants of them were gingivitis and 15 chronic periodontitis) **(OPg, OPp).**

Investigations of full clinical periodontal parameters (PLI, GI, BOP, PPD and CAL) were done by:

1. Assessment of soft deposits by Plaque index (PLI) **21.**
2. Assessment of Gingival Inflammation by Gingival index (GI) **22.**
3. Assessment of Bleeding on probing (BOP) **3.**
4. Assessment of Probing Pocket Depth (PPD) **3.**
5. Assessment of Clinical attachment level (CAL).

Statistical analysis was done using mean, median, Min, Max, SD, SE, percentages, Kruskal-Wallis H test, Mann-Whitney U test, Chi-square test, Dun test with control, Spearman's rank correlation coefficient test (r).

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RESULTS

The present study showed that the median values of PLI were highest in ALN group(2.06) than that of both control and OP group (0.73,1.88) respectively with highly significant difference between them and in multiple comparisons of groups (MC of Groups)except between the last two groups there was statistically not significant difference, the highest median value of GI was in OP group (1.84) followed by control then ALN group (0.61, 1.07) respectively with highly significant difference between them , in intra groups comparisons the OP group were higher than that in ALN group(1.80,1.11,1.90,1.06) respectively with highly significant difference between them, regarding inter group comparisons the GI of ALN group is higher in gingivitis than in periodontitis with no significant difference, while in OP group the opposite is true. Mean percentage of BOP score 1 in OP group (59.20) higher than that of ALN group (12.90) and in gingivitis group (40.33) higher than that of periodontitis group (31.77), in intra comparison in ALN group and OP group, the mean percentage of BOP score 1 were higher in gingivitis group than periodontitis one(14.21,11.58,66.44,51.97) respectively, while intercomparison, the gingivitis and periodontitis in OP group were higher than those of ALN group with highly significant difference . Median value of PPD in ALNp sub group is (4.29) that is lower than that of OPp sub group (6.40) with highly significant difference between them. Regarding CAL mean value in ALNp sub group is lower than that of OPp sub group (5.23, 6.93) respectively with highly significant difference between them. Spearman's Correlation Coefficient showed that total correlation between drug intake duration and clinical periodontal parameters were weak negative non significant with (BOP, PPD, CAL) except for (PLI, GI) there were strong positive highly significant and weak positive highly significant correlation respectively between them.

Table1: Descriptive and analytic statistics of PLI parameter with inter group comparisons Mann-Whitney U test among the study and control groups.

Statistic	Group#			Gingivitis		Periodontitis		Inter groups comparisons			
	Control [1]	ALN[2]	OP[3]	ALN	OP	ALN	OP	ALNg	ALNp	OPg	OPp
Med	.73	2.06	1.88	2.11	1.88	2.02	1.88	2.11	2.02	1.88	1.88
MR	15.50	68.18	52.82	19.87	11.13	18.83	12.17	15.53	15.47	15.87	15.13
Statistic	X^2=64.547 P=0.000 HS			Z=2.717 P=0.006 HS		Z=2.075 P=0.037 S		Z=0.021 P=1.00 NS		Z=0.228 P=0.838 NS	

#=Kruskall-Wallis (Chi-square), df=2, Z= Mann-Whitney U test

Table2: Multiple comparisons of Groups for PLI parameter and Dun test for multiple comparisons of sub groups with control.

MC of Groups	Groups	Z	P
	1 X 2	7.81	0.000
	1 X3	5.53	0.000
	2 X3	2.28	0.068

Dun test with control						
MC with control	StatisticalTest	Comparison		MR	Z	P-value	Sig.
	(Chi- square) = 64.593	MR= 15.50	ALNg	68.57	6.424	0.000	HS
	Df=4	Control	ALNp	67.80	6.323	0.000	HS
	P=0.000		OPg	52.50	4.470	0.000	HS
	HS		OPp	53.13	4.555	0.000	HS

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Table3: Descriptive and analytic statistics of GI with inter group comparisons Mann-Whitney U test among the study and control group.

Statistic	Group#			Gingivitis		Periodontitis		Inter groups comparisons			
	Control[1]	ALN[2]	OP[3]	ALN	OP	ALN	OP	ALNg	ALNp	OPg	OPp
Med.	.61	1.07	1.84	1.11	1.80	1.06	1.90	1.11	1.06	1.80	1.90
MR	15.50	45.50	75.50	8.00	23.00	8.00	23.00	16.80	14.20	12.13	18.87
Statistics	X^2=79.123, P=0.000 (HS)			Z=4.666 P=0.000 (HS)		Z=4.666 P=0.000 (HS)		Z=0.809 P=0.436 (NS)		Z=2.095 P=0.037 (S.)	

#=Kruskall-Wallis (Chi-square),df=2,Z=Mann-Whitney U test

Table4: Multiple comparisons of Groups for GI and Dun test of study groups with control.

MC of Groups	Groups	Z	P
	1 X 2	4.45	0.000
	1 X3	8.895	0.000
	2 X3	4.45	0.000

Dun test with control							
MC with control	StatisticalTest	Comparison		MR	Z	P-value	Sig.
	(Chi-square)= 79.695	MR=15.50	ALNg	46.80	3.816	0.0005	HS
	Df=4	Control	ALNp	44.20	3.437	0.0024	HS
	P=0.000		OPg	72.13	6.851	0.000	HS
	HS		OPp	78.87	7.666	0.000	HS

Table 5: Mean percentage of BOP scores 1 with comparison of Mean in gingivitis and periodontitis in ALN and OP group.

%Scores	Groups	Subgroup	Mean	±SD
1	ALN	Gingivitis	14.21	4.02
		Periodontitis	11.58	5.12
		Total	12.90	4.72
	OP	Gingivitis	66.44	3.86
		Periodontitis	51.97	7.18
		Total	59.20	9.29
	Total	Gingivitis	40.33	26.84
		Periodontitis	31.77	21.43

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Table 6: Descriptive statistics and Mann-Whitney U test of PPD parameter for ALNp and OPp subgroups.

Descriptive	ALNp	OPp	Mann-Whitney U Test	
			Z	P-value
Min.	4.00	5.40	4.068	0.000
Max.	6.20	8.57		
Mean	4.77	6.41		
±SD	.80	.73		
Med.	4.29	6.40		
MR	8.97	22.03		

Table 7: Descriptive statistic and Mean value of CAL parameter for ALNp and OPp sub groups with Independent T- test.

Descriptive	ALNp	OPp	T	Independent Sample T-test	
				df	P-value
Min.	4.00	5.40	5.519	22.644	.000
Max.	6.10	8.38			
Mean	5.23	6.93			
±SD	.61	1.03			

Table 8: Correlation between Drug intake duration and clinical periodontal parameters in ALN group

Subgroups		Drug intake	
		r	P-value
ALNg	PLI	.263	.343
	GI	**-.866**	**.000**
	BOP score1	-.124	.659
	PPD	.	.
	CAL	.	.
ALNp	PLI	**-.559**	**.030**
	GI	**-.768**	**.001**
	BOP score1	-.140	.618
	PPD	-.351-	.200
	CAL	.158	.573
Total	PLI	**.579**	**.000**
	GI	**.470**	**.000**
	BOP score1	-.146	.264
	PPD	-.078	.683
	CAL	-.016	.934

DISCUSSION

Periodontal disease is very widespread in the population with age range similar to those affected by osteoporosis [**23].** Many researchers have suggested an association between PD and osteoporosis in postmenopausal women [**24].** Dental plaque is the major etiological factor in periodontal diseases. The

bacterial aggregation leads to formation of microbial biofilm and bacterial invasion which result in destruction of the periodontium thus enhance plaque accumulation on the teeth surfaces **3.** After menopause salivary flow rate will be decreased and salivary composition may be altered, contributing to the development of several oral conditions [**25].**In addition to change in the buffering capability of saliva resulting in variation in microbial flora these influences produce greater accumulation of dental plaque [**2].** Possible explanation for the results in current study that females at postmenopausal period experience diverse physical and emotional symptoms ,change in dietary patterns, and many oral changes which are frequently found among these women. There is also higher prevalence of periodontal disease and osteoporotic jaws [**26].**Also oral hygiene status is influence by many other factors such as host susceptibility to dental plaque, nutritional habits, educational and socioeconomic status. It was reported that postmenopausal women with osteoporosis and periodontitis are really susceptible to excessive response to dental plaque and calculus, [**27].**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[**4**].ALN affects production of cytokine by cells of immune system in vitro [**28].**It was also confirmed to exert anti inflammatory and anti bacterial actions in experimental periodontitis ,in addition to hinder the neutrophil arrival and other important immune cells in host defense mechanism against bacterial infection which has been connected to tissue damage in many inflammatory diseases such as PD. It was also able of dropping penetration of mononuclear cell in gingival tissue**,** additionally it was able of hindering the ability of macrophages to produce proinflammatory cytokines[**29]**.The significant variation in clinical inflammation of periodontal tissues after ALN treatment imply less significant destruction of periodontal tissue which may be due to reduction of collagen breakdown possibly by inhibitory action of ALN on tissue matrix metalloproteinase which breakdown periodontal component, and have major functions in tissue healing and immunity which considered of great clinical importance in PD through activation of cytokines and other effector molecules, that play significant roles in wound healing as well as in inflammation [**30].** ALN was established of averting periodontal ligament devastation [**31,32]** and conserve alveolar bone via its anti-inflammatory and antibacterial behavior in experimental periodontitis [**24].**At the initiation of resorption process by osteoclast it attach to the bone mineral, and liberated owing to greatly acidic local milieu. This will then capture by osteoclast leading to either obstructing of their development from hematopoietic precursors, stimulation of apoptosis, or diminution of activity. Different studies demonstrated that the systemically used ALN in humans as well as some animal models declined bone loss and improve bone density owing to the fact that ALN is a powerful bone resorption inhibitor **[31],** it attaches to hydroxyapatite crystals and stop their dissolution, this feature guiding for use of ALN as a host modulating issue in an attempt to avert alveolar bone loss in PD**.** Also it has been revealed to enhance collagen and osteocalcin synthesis via bone cells, impairment of intracellular collagenolysis along with proteoglycans synthesis via cartilage cells and increased fibroblast growth factor construction; accordingly it may perhaps, under certain conditions, ever-increasing bone formation.[**33].** Lake of correlation between ALN intake and some clinical periodontal parameters could be attributed to short duration of drug intake that mask or not be able to clarify the beneficial outcome of drug on periodontium and confounding of results by most important factor which is host response to dental plaque and oral hygiene condition.

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