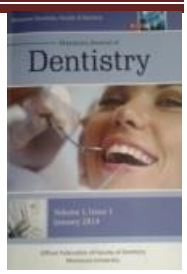
The Effect of Alendronate gel (1%) in combination with Hydroxyapatite (HA) in regeneration of periodontal defects in periodontitis patients (Clinically and Radiographically).



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Abstract:

Objectives: The aim of the present study is to evaluate the effect of Alendronate gel (1%) in combination with Hydroxyapatite (HA) in regeneration of periodontal defects in periodontitis patients (Clinically and Radiographically).

Patients and methods: Fourty patients diagnosed as stage III & grade B periodontitis with vertical bony defects and showed radiographic bone loss ≥5mm were selected from periodontology and oral medicine department faculty of dentistry Mansoura University. The patients were divided into four groups. Group (I) composed of ten patients treated with combination of Alendronate gel (1%) with Hydroxyapatite bone graft (HA) with periodontal flap surgery. Group (II) composed of ten patients treated with Alendronate gel (1%) alone with periodontal flap surgery, group (III) composed of ten patients treated with Hydroxyapatite bone graft (HA) alone with periodontal flap surgery. Group (IV) composed of ten patients treated by open flap debridement using minimally invasive surgical technique. Clinical periodontal parameters (plaque index PI, gingival index GI, clinical probing depth PD, clinical attachment level CAL) were taken from each patients at baseline and 6 months after treatment. Periapical radiographs were taken for each patient to evaluate the radiographic bone level change before and after treatment. The radiographs were taken at baseline and 6 months from surgery.

Results: Clinical periodontal parameters were significantly improved after treatment in all treatment groups compared to the baseline. Regarding bone level there was gain in the bone level after treatment in all treatment groups with significant improvement in group I (ALN gel 1% + HA). There was a statistically significant difference among the treatment groups between the base line and after 6 months from surgery (p value ≤0.05).

Conclusions: Combination of Alendronate gel (1%) and Hydroxyapatite (HA) gave good results in the treatment outcomes as regard bone level and periodontal clinical parameters.

Keywords: *Periodontal regeneration, vertical bone loss, Alendronate gel , Hydroxyapatite bone grafting material.*

Introduction

Periodontitis is an inflammatory disease of the supporting tissues of teeth caused by an array of microorganisms, resulting in progressive destruction of periodontal ligament and alveolar bone with pocket formation, recession or both.(1)Intra-ossseous periodontal defects are at a higher risk of disease progression when left untreated.(2)

Although periodontitis is initiated by bacterial colonization, host response plays an essential role in the breakdown of tissue and bone.(3) The prevention of bone loss associated with periodontitis through host-response modulation may be an effective adjuvant treatment associated with SRP. Thus, the use of anti-resorptive drugs may provide an effective alternative adjuvant therapy for periodontitis.(4)Hence, pharmacological agents, like bisphosphonates, which modulate host responses are being tested as treatment modalities for periodontal lesions.(5)

Alendronate (ALN), an aminobisphosphonate is a potent inhibitor of osteoclast-mediated bone resorption with no adverse effect on the mineralization of bone. (6)The effectiveness of ALN in reducing alveolar bone resorption after mucoperiosteal flap surgery has been demonstrated in various studies.(7)

Bisphosphonates play an important role in accelerating bone formation as it stimulates osteogenesis in conjunction with regenerative materials around osseous defects.(1) A variety of grafting materialshave been used in bone grafting for the treatment of periodontal defects to obtain periodontal tissue regeneration.(8)

It has been shown that Hydroxyapatite (HA) bone grafts have excellent bone-conductive properties which permit outgrowth of osteogenic cells from existing bone surfaces into adjacent bone graft material.(9) Due to the effectiveness of ALN in reducing alveolar bone resorption and due to the advantages of hydroxyapatite (HA) bone grafting material in guided tissue regeneration (GTR), it was worth using both materials in order to obtain better results in treatment of periodontal defects.

Aim of the study:

to evaluate the Effect of Alendronate gel (1%) in combination with Hydroxyapatite (HA) in regeneration of periodontal defects in periodontitis patients (Clinically and Radiographically).

Patients and methods:

A total of fourty patients with the following inclusion criteria: Patients of both sexes between 40 and 55 years old . Individuals with probing depth ≥5mm. Individuals with clinical attachment loss ≥ 5mm. Individuals with vertical bony defects. Smokers, pregnant women ,patients with systemic diseases, drug abusers and uncontrolled diabetic patients were excluded from the study. The patients were diagnosed as stage III & grade B periodontitis and showed radiographic bone loss ≥5mm. The patients were divided into four treatment groups.

Group (I):Included ten patients using Alendronate gel (1%) with Hydroxyapatite bone graft (HA) and mixed together and used as a bone grafting material for vertical bony defect regeneration during surgery.

Group (II):Included ten patients using Alendronate gel (1%) alone as a regenerative material for vertical bony defect regeneration during surgery.

Group (III):Included ten patients using Hydroxyapatite (HA) alone as an alloplastic bone substitute's material for vertical bony defect regeneration during surgery.

Group (IV):Included ten patients, Periodontal flap surgery was performed alone by minimally invasive surgical technique.

Before any surgical procedures Phase (I) periodontal therapy consisted of debridement, scaling and root planning to remove all supragingival and subgingival deposits (plaque and calculus) and oral hygiene instructions were given to the patients in the form of teeth brushing, flossing and chlorohexidine mouth wash. Clinical assessment of situation after Phase I therapy were conducted to assess improvement in clinical signs and symptoms.

Aseptic field was required for all surgical procedures using povidine iodine. Local anesthesia using 4% articane with 1:100.000 epinephrines was applied for buccal infiltration injection of 1.5 ml and palatal infiltration injection of 0.3 ml. Inferior alveolar nerve block and Lingual nerve block were used for mandibular posterior segment.

All surgical procedures were performed using minimally invasive surgical technique. Blade number 15 was used to reach to infrabony defects through horizontal or oblique incisions at the base of the buccal papilla. Flap was extended mesiodistally and was modified according to the defect geometry then full thickness buccal flap was elevated to evaluate the periodontal defect. The interdental tissues were separated from underlying bone using sharp micro blade. The interdental tissue might be rolled at palatal side with full thickness flap if the periodontal defects reached to the palatal site.

All granulation tissues into the periodontal defect were removed using sharp micro scalers and curettes, then flushing of the defect with ultrasonic scaler. Then different regenerative materials were applied and packed into the periodontal defects according to the different treatment groups. Group (I) treated with combination of Alendronate gel (1%) and Hydroxyapatite bone grafting material (HA). Group (II) treated with Alendronate gel (1%) alone and group (III) treated with HA alone. Group (IV) involved open flap debridement through minimally invasive surgical technique. Then intimate wound closure was conducted and post-operative medications and instructions were given to the patients.

Analytical statistics:

Data management and statistical analysis were performed using the Statistical Package for Social Sciences (SPSS) version 24. Numerical data were summarized using means and standard deviations or medians and ranges. Data were explored for normality using Kolmogrov-Smirnov test and Shapiro-Wilk test.

Categorical data were summarized as percentages. Comparisons between the 4 groups with respect to normally distributed numeric variables were done using the ANOVA test followed by Bonferroni post hoc test. None normally distributed numeric variables were compared by Kruskal Wallis test. Comparison overtime was done by paired t test and its non-parametric analogue Wilcoxon signed rank test as appropriate.

All p-values are two-sided. P-values ≤ 0.05 were considered significant.

Results:

In **Group I** (ALN 1% gel + HA) the mean value of plaque index (PI) at the baseline before surgery was 2.6±0.5, while after 6 months it was 0.6±0.5. The mean value of gingival index (GI) at the baseline before surgery was 2.7±0.7, while after 6 months it was 0.8±0.6. The mean value of clinical probing depth (PD) at the baseline was 7.4±1.1, while after 6 months it was 5.2±1.2. The mean value of clinical attachment level (CAL) at the baseline before surgery was 7.5±1.2, while after 6 months it was 5.3±1.3. The mean value of the amount of bone gain in group (I) was 2.2±0.6mm.

In **Group II** (ALN 1% gel) the mean value of plaque index (PI) at the baseline before surgery was 2.5±0.5, while after 6 months it was 0.9±0.6. The mean value of gingival index (GI) at the baseline before surgery was 2.7±0.5, while after 6 months it was 0.9±0.7. The mean value of clinical probing depth (PD) at the baseline was 7.3±0.9, while after 6 months it was 5.3±1. The mean value of clinical attachment level (CAL) at the baseline before surgery was 7.4±0.9, while after 6 months it was 5.5±0.8. The mean value of the amount of bone gain in group (II) was 1.7±0.4 mm.

In **Group III** (HA) the mean value of plaque index (PI) at the baseline before surgery was 2.6±0.5, while after 6 months it was 1.0±0.7. The mean value of gingival index (GI) at the baseline before surgery was 2.6±0.5, while after 6 months it was 0.8±0.6. The mean value of clinical probing depth (PD) at the baseline was 7.9±0.9, while after 6 months it was 6 ±0.8. The mean value of clinical attachment level (CAL) at the baseline before surgery was 8.1±0.8, while after 6 months it was 6.2±0.9. The mean value of the amount of bone gain in group (III) was 1.9±0.7 mm.

In **Group IV** (Minimally invasive surgical technique) the mean value of plaque index (PI) at the baseline before surgery was 2.7±0.5, while after 6 months it was 0.8±0.7. The mean value of gingival index (GI) at the baseline before surgery was 2.7±0.5, while after 6 months it was 0.8±0.8. The mean value of clinical probing depth (PD) at the baseline was 7.5±1.1, while after 6 months it was 7±1.1. The mean value of clinical attachment level (CAL) at the baseline before surgery was 7.5±0.9, while after 6 months it was 6.9±1.1. The mean value of the amount of bone gain in group (IV) was 0.7±0.6 mm.

Discussion:

The goal of regenerative periodontal therapy is to restore the supporting structures of periodontium that were damaged due to periodontitis.(10) Many treatment modalities have been used through years to treat periodontal defects starting from non-surgical periodontal therapy to surgical periodontal therapy. Later on guided tissue regeneration has been adopted and biologic mediators and barrier membranes have been incorporated into the process.(11)

The purpose of the present study is to evaluate clinically and radiographically the effect of Alendronate gel (1%) in combination with Hydroxyapatite (HA) in treatment of vertical bone loss in periodontitis patients. Due to the effectiveness of ALN in reducing alveolar bone resorption and due to the advantages of hydroxyapatite (HA) bone grafting material which is an important factor for an osteoinductive property and act as scaffold on which the new bone grew in guided tissue regeneration (GTR).There were no adverse reaction or any risk associated with the study and the patients reported little post-operative pain and discomfort which was controlled with analgesics and anti-inflammatory drugs that were prescribed to them.

In our study bone level showed significant increase after 6 months as compared to the baseline in Group I [table 1] .that could be due to the superior osteoinductivity as well as osteconductivity with better new bone formation within both materials ALN gel (1%) and HA (12) . The properties of ALN gel (1%) gave that combination perfect remodeling behavior and resorption time to be replaced with the host bone. These results came in agreement with **Rohini Naineni, Vishali Ravi** (13) who studied the effect of Alendronate with Bone Substitute in Surgical Therapy of Periodontal Intra-Osseous Defects.

Bone level showed significant increase after 6 months as compared to the baseline in Group II [table5] .This could be related also to the inhibition of resorptive activity is thought to

produce a shift in bone turnover equilibrium to more osteoblastic activity.(14) This was consistent with **Öz UC, Toptaş M, K et.al** (15) who showed enhancement bone regenaration activity after application of Alendronate gel in bony defects . Also bone level showed significant increase after 6 months as compared to the baseline in Group III [table5]. This could be due to the the structure of HA is an important factor for an osteoinductive property and act as scaffold on which the new bone grew. This was in agreement with **Kattimani VS, Franceschini Neto F** (16, 17) who tested the repair of bony defects using HA and showed improved results. Regarding group IV there was a limited improvement in the bone level after 6 months as compared to the baseline [table5]. This was in agreement with **Ortiz et al.** (18) who used minimal flap to correct periodontal bony defects and showed questionable results regarding bone level gain..

Conclusion:

Based on the results of the study it can be concluded that:The use of Alendronate gel (1%) mixed with Hydroxyapatite (HA) bone graft was found to be effective in stimulation of new bone formation for regeneration of vertical bony defect. The application of Alendronate gel (1%) alone as a regenerative material in vertical bony defect gave a marked improvement in bone level gain and periodontal clinical parameters. Although Hydroxyapatite (HA) showed good results as regard improving bone level and periodontal clinical parameters, but it was not as effective as when it was applied in combination with Alendronate gel (1%).

Table (1): Mean, Standard deviation, median and range of Plaque index at the baseline and after 6 months:

	Plaque index				
	Baseline		6 Months		
	Mean ±SD	Median(Range)	Mean ±SD	Median(Range)	p value1
Group I	2.6±0.5	3.0(2-3)	0.6±0.5	1.0(0-1)	0.003
Group II	2.5±0.5	2.5(2-3)	0.9±0.6	1.0(0-2)	0.004
Group III	2.6±0.5	3.0(2-3)	1.0±0.7	1.0(0-2)	0.004
Group IV	2.7±0.5	3.0(2-3)	0.8±0.7	1.0(0-2)	0.004
p value 2	0.846		0.550		

SD: standard deviation, p≤ 0.05 is significant, p value 1 for comparing baseline with 6 months (overtime) in each single group done by Wilcoxon signed rank test, p value2: for comparing between groups at different time points done by Kruskal Wallis test.

Table (2): Mean, Standard deviation, median and range of gingival index at the baseline and after 6 months:

	Gingival Index				
	Baseline		6 Months		
	Mean ±SD	Median(Range)	Mean ±SD	Median(Range)	p value1
Group I	2.7±0.7	3.0(1-3)	0.8±0.6	1.0(0-2)	0.004
Group II	2.7±0.5	3.0(2-3)	0.9±0.7	1.0(0-2)	0.004
Group III	2.6±0.5	3.0(2-3)	0.8±0.6	1.0(0-2)	0.004
Group IV	2.7±0.5	3.0(2-3)	0.8±0.8	1.0(0-2)	0.004
p value 2	0.841		0.985		

SD: standard deviation, p≤ 0.05 is significant, p value 1 for comparing baseline with 6 months (overtime) in each single group done by Wilcoxon signed rank test, p value2: for comparing between groups at different time points done by Kruskal Wallis test.

Table (3): Mean, Standard deviation of Probing depth in the studied groups:

	Periodontal Probing Depth (mm)				
	Baseline		6 Months		
	Mean	SD	Mean	SD	p value1
Group I	7.4	1.1	5.2[a]	1.2	<0.001
Group II	7.3	0.9	5.3[b]	1.0	<0.001
Group III	7.9	0.9	6.0[c]	0.8	<0.001
Group IV	7.5	1.0	7.0[a-b-c]	1.1	0.001
p value2	0.611		0.002		

SD: standard deviation, p≤ 0.05 is significant p value 1 for comparing baseline with 6 months (overtime) in each single group done by paired t test, p value2: for comparing between groups at different time points done by ANOVA test followed by Bonferroni post hoc test, similar letters are statistically significant.

Table (4): Mean, Standard deviation of Clinical Attachment Level in the studied groups at baseline and after 6 months:

	Clinical Attachment Level (mm)				
	Baseline		6 Months		
	Mean	SD	Mean	SD	p value1
Group I	7.5	1.2	5.3[a]	1.3	<0.001
Group II	7.4	0.9	5.5[b]	0.8	<0.001
Group III	8.1	0.8	6.2	0.9	<0.001
Group IV	7.5	0.9	6.9[a-b]	1.1	0.009
p value2	0.477		0.004		

SD: standard deviation, p≤ 0.05 is significant p value 1 for comparing baseline with 6 months (overtime) in each single group done by paired t test, p value2: for comparing between groups at different time points done by ANOVA test followed by Bonferroni post hoc test, similar letters are statistically significant.

Table (5): Mean, Standard deviation of bone gain Level in the studied groups:

	Group I		Group II		Group III		Group IV		
	Mean	SD	Mean	SD	Mean	SD	Mean	SD	P value
BG	2.2[a]	0.6	1.7[b]	0.4	1.9[c]	0.7	0.7[a-b-c]	0.6	<0.001

SD: standard deviation, p≤ 0.05 is statistically significant, similar letters are statistically significant, analysis done by one way ANOVA followed by Bonferroni post hoc test, similar letters are statistically significant

Case of Group(I)

Fig.1. showed infra bony defect related to the distal surface of lower right first molar of the patient.

Fig.2. showed bone graft material (ALN gel(1%)+HA) into the periodontal bony defect.

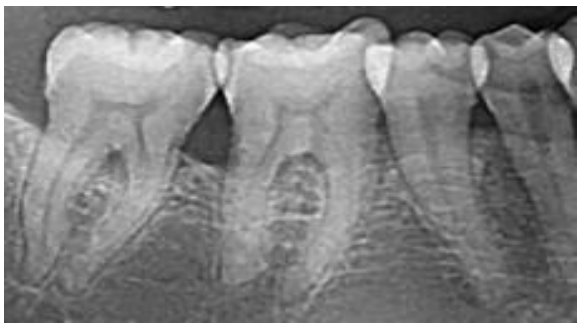

Fig.3. periapical radiograph showed the bone loss at the baseline before the treatment.

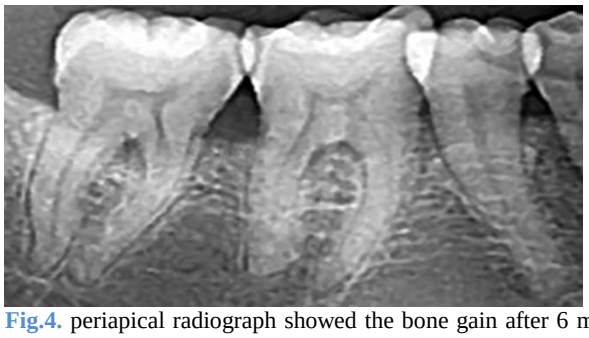

Fig.4. periapical radiograph showed the bone gain after 6 months after treatment.

Case of Group (II)

Fig.5. showed infra bony defect related to the mesial surface of upper right first molar of the patient.

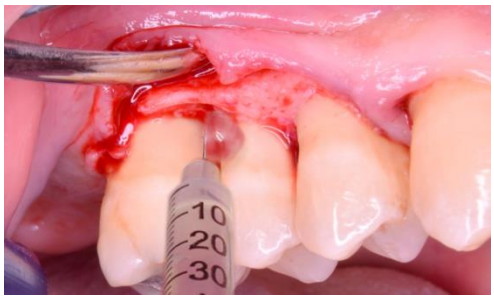

Fig.6. showed application of ALN gel(1%) into the periodontal bony defect.

Fig.7. periapical radiograph showed the bone loss at the baseline before the treatment.

Fig.8. periapical radiograph showed the bone gain after 6 months after treatment.

Case of Group (III)

Fig.9. showed infra bony defect related to the distal surface of lower left first molar of the patient.

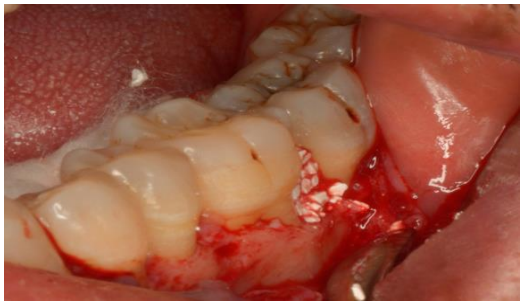

Fig.10. showed (HA) bone graft material into the periodontal bony defect.

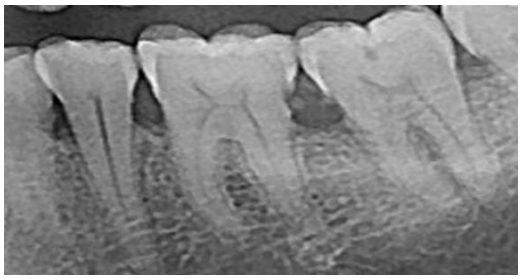

Fig.11. periapical radiograph showed the bone loss at the baseline before the treatment.

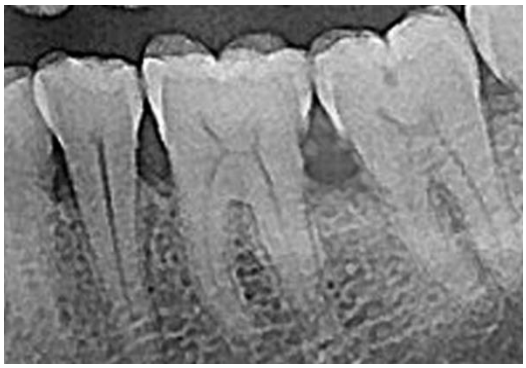

Fig.12. periapical radiograph showed the bone gain after 6 months after treatment.

Case of Group (IV)

Fig.13. showed infra bony defect related to the distal surface of upper right first molar of the patient.

Fig.14.showed simple interrupted sutures of the upper right side of the patient.

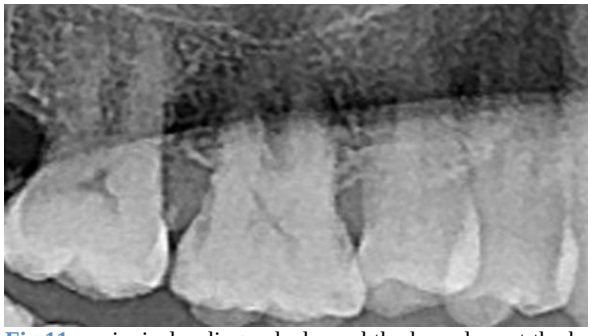

Fig.11. periapical radiograph showed the bone loss at the baseline before the treatment.

Fig.12. periapical radiograph showed the bone gain after 6 months after treatment.

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