

Role of Alendronate Gel versus Chlorhexidine Gel as Adjunct to Mechanical Therapy in Treatment of Chronic Periodontitis (Clinical and Microbiological Study)

Ahmed M. El-Hadidy¹, Bassant H. Mowafy², Medhat El-Daker³, Una M. El-Shinnawi⁴

Abstract:

Objective: Background: This study evaluated the clinical and microbiological efficacy of Alendronate (ALN) gel versus Chlorhexidine (CHX) gel as an adjunct to mechanical therapy in the treatment of chronic periodontitis and compared this effect with Scaling and Root Planning (SRP) only. **Materials and Methods:** Forty patients with chronic periodontitis were randomly allocated into two groups. Each group of twenty patients was split into a study group and a control group, group 1 was treated on one side with ALN gel after (SRP) and the other side was treated with (SRP) only. group 2 was treated on one side with CHX gel after (SRP) and the other side was treated with (SRP) only. Clinical parameters such as plaque index (PI), clinical attachment level (CAL), probing depth (PD), sulcus bleeding index (SBI), and microbiological assessment as total bacterial count, prevotella intermedia, porphyromonas gingivalis were evaluated after three months. **Results:** It has been shown that there was a significant difference in clinical and microbiological assessment for all groups when comparing pre-treatment measurements vs post-three months treatment measurements. While there was no significant difference in both clinical and microbiological assessment after three months when comparing treatment groups of alendronates after SRP vs CHX after SRP. **Conclusion:** Considering the clinical and microbiological relevance, local application of either ALN gel or CHX gel is considered a valid adjunctive therapy to SRP.

Introduction:

Periodontitis is an infection-driven inflammatory disease in which the composition of biofilms plays a significant character. Dental plaque accumulation at the gingival margin initiates an inflammatory response that, in turn, causes microbial alterations and may lead to drastic consequences in the periodontium of susceptible individuals¹.

Treatment of chronic periodontitis is still a challenge. Conventional periodontal therapy aims to reduce or eradicate periodontal pathogens. SRP is a basic part of the first phase in periodontal therapy and leads to significant improvement in the clinical parameters². However, SRP may fail to eliminate the subgingival bacteria located in areas such as deep pockets which are inaccessible to periodontal instruments, multi-rooted teeth, furcation, gingival tissue, concavities, and interproximal areas³.

Since antimicrobials overcome the technical limitations of mechanical treatment, prevent early recolonization of microorganisms, and provide the best conditions for clinical improvement, local or systemic antimicrobials have been introduced in the treatment of periodontal disease, as an adjunctive measure⁴.

Alendronate sodium is an amino bisphosphonate that acts as an anti-osteolytic agent. ALN binds to resorptive surfaces and is locally released during the acidification associated with the osteoclastic activity resulting in an alteration in the ruffled border membrane characteristic of osteoclasts without destroying the cells. Therefore, ALN

seems to have the potential to be used as an inhibitor of alveolar bone resorption in the treatment of periodontitis⁵.

Chlorhexidine (CHX), which is one of the most investigated antiseptics, yielded a great effect against Gram-positive and Gram-negative bacteria, viruses, and yeast. To accomplish its activity in the periodontal pocket area, CHX must reach the site of action and remain at an adequate concentration long enough for its pharmacological effect to occur⁶.

Hence, this study was designed to evaluate clinical and microbiological efficacy of alendronate gel versus chlorhexidine gel as adjunct to mechanical therapy in treatment of chronic periodontitis.

Materials and Methods:

I) Patient selection:

The sample size was calculated by the G*power software program, for which the outcome of interest was measuring probing depths (PDs) among patients with chronic periodontitis. This sample size was calculated based on the following assumptions: mean±SD of PD at 2 months among Alendronate group treated with SRP followed by a 1% ALN gel (10 mg/mL) local drug delivery was 4.39±1.45 while, that among placebo group treated with SRP followed by placebo-gel placement was 5.88±1.78⁷; α -error probability was 0.05; power (1- β error probability) was 0.80. The calculated sample size was 20 for each group and the total sample size was 40.

A total of Forty patients were diagnosed with chronic periodontitis were selected from the Department of Oral Medicine, Periodontology, Oral Diagnosis and Radiology, Faculty of Dentistry, Mansoura University.

All the patients had all the information available about the treatment including the possible effects or risks, and other treatment options. All the patients give written consent before performing any required steps.

¹Postgraduate MSc student, Department of Oral Medicine and Periodontology, Faculty of Dentistry, Mansoura University, Egypt. ahmed.elhadidy.93@gmail.com

²Assistant professor, Department of Oral Medicine, Periodontology, Diagnosis and Oral Radiology, Faculty of Dentistry, Mansoura University, Egypt.

³Professor, Department of Medical Microbiology and Immunology, Faculty of Medicine, Mansoura University, Egypt.

⁴Professor, Department of Oral Medicine, Periodontology, Diagnosis and Oral Radiology, Faculty of Dentistry, Mansoura University, Egypt.

The proposal of the study was approved by the Dental Research Ethics Committee, Faculty of Dentistry, Mansoura University (Reference number M.S.A09150620).

(II) Inclusion criteria:

Chronic periodontitis patients above 30 years old (Both Gender).

Individuals with probing depth ≥ 4 mm.

No history of antibiotic and periodontal therapy in the last 3 months.

(III) Exclusion criteria:

- Smokers.
- Pregnant or lactating mothers.
- History of systemic diseases.

(IV) Clinical Parameters: The periodontal evaluation was performed including the following parameters:

1. Plaque index (PI)⁸
2. Clinical Attachment Level (CAL)⁹
3. Probing Depth (PD)¹⁰
4. Sulcus Bleeding Index (SBI)¹¹

(V) Study design:

All patients were randomly (by a computer-generated system) assigned to either the ALN or CHX group, then a split-mouth design was applied in each group. For every single patient, one side was assigned randomly (by a computer-generated system) to be the test site and the opposite side to be the control site.

(VI) Study groups: All patients were divided as follow:

Group (I) consisted of twenty patients who were treated with (ALN) gel after SRP on the test side while the control side was treated with SRP only.

Group (II): consisted of twenty patients who were treated with, 10 mg Chlorhexidine Digluconate (Chlorohexidine gel EZ-Cure) after SRP on the test side while the control side was treated with SRP only.

(VIII) Treatment Plan:

The Probing depth, plaque, and gingival indices were recorded for both groups at the first visit.

The subgingival plaque sample was gathered from 2 sites with deep pockets by the following technique:

After proper isolation, the supragingival plaque was removed with a sterile curette to avoid contamination between supragingival and subgingival plaque, and excess saliva was removed.

The subgingival plaque samples were collected by inserting 2 sterile medium-sizes endodontic paper points into the pocket for 15 seconds.

After that, the paper points were immediately stored in a sterile vial containing 1.5 ml of microcentrifuge tube thyoglycolate broth transport media and sent immediately to Microbial Diagnostic and Infection Control Unit (MDICU) for sample processing. Samples were cultured

anaerobically for detection of total bacterial count as well as *p.gingivalis* and *p.intermedia*.

Scaling and Root Planning:

After plaque sampling, the heavy calculus deposits were removed as not to interfere with the insertion of the probe. Then PD and CAL were measured for both groups.

Full mouth disinfection through SRP was performed over two weeks till establishing a smooth crown and root surfaces and oral hygiene instructions were given carefully at each appointment.

Application of ALN gel for group I and Chlorhexidine gel for group II were done by the following procedure:

The gel was applied subgingivally in the deepest selected periodontal pockets in the selected quadrant using a disposable plastic syringe.

After proper isolation, the gel was applied carefully subgingivally and interproximal until the excess gel was observed from the gingival margin. This procedure was repeated, and the excess gel was removed using a cotton roll. The patients were instructed not to eat, drink, or rinse for at least one hour.

Gel application was performed once a week for six weeks and any supragingival deposits were removed at recall visits.

Post-operative assessment: The subgingival plaque sample was recollected. Probing depth, plaque, and gingival indices were remeasured for both groups after 3 months.

(VII) Microbiological assessment: Transported samples were cultured semi-quantitatively on three bacterial media. Brain heart infusion (BHI) agar (Oxoid) for detection of total bacteria count. Brain heart infusion (BHI) agar supplemented with 5.0 ug/ml hemin for detection of *Porphyromonas gingivalis*. Blood agar containing 10 mg sulphamethoxazole/L and 0.5 mg trimethoprim/L for detection of *Prevotella intermedia*.

Results:

The patients were divided into two equal groups (CHX group and ALN group). In the CHX group, the patients receive SRP on one side and combined SRP with CHX gel on the other side. Similarly done with ALN group. There was no statistically significant difference between study groups regarding their mean age and sex.

Concerning PI, CAL, and PPD; There was no statistically significant difference between studied groups either pre-treatment or post-treatment. While comparing pre-and post-treatment values demonstrated a statistically significantly lower mean value among all studied groups.

Related to the gingival bleeding index, all cases with positive pre-treatment index turned into negative post-treatment.

About total bacterial count (TBC), *Prevotella intermedia* (PI), and *porphyromonas gingivalis* (PG); There was no statistically significant difference between studied groups either pre-treatment or post-treatment. While comparing pre-post treatment values demonstrated significant lowering TBC mean within each group.

Table (1): Clinical parameters of study participants

Clinical parameters		Alendronate group		Chlorohexidine group		p-value@
		ALN gel with SRP (n=20) Mean±SD	SRP (n=20) Mean±SD	CHX gel with SRP (n=20) Mean±SD	SRP (n=20) Mean±SD	
PI	Baseline	2.6±0.5	2.7±0.5	2.5±0.5	2.6±0.5	0.7
	After 3 months	0.5±0.5	0.6±0.5	0.5±0.5	0.6±0.50	0.9
	p-value*	<0.001	<0.001	<0.001	<0.001	
CAL	Baseline	4.6±0.6	4.7±0.8	4.5±0.9	4.8±0.6	0.4
	After 3 months	2.3±0.7	2.4±0.7	2.2±0.8	2.5±0.7	0.6
	p-value*	<0.001	<0.001	<0.001	<0.001	
PD	Baseline	5.1±1.0	4.8±0.9	5.0±0.8	5.2±0.6	0.3
	After 3 months	2.5±0.6	2.9±0.9	2.4±0.8	2.7±0.8	0.2
	p-value*	<0.001	<0.001	<0.001	<0.001	

@: One-Way ANOVA test between groups, *: paired T-test within each group baseline vs follow up, PI: Plaque Index, CAL: periodo Level, PPD: Periodontal Pocket Depth

Table (2): Microbiological parameters of study participants

Microbiology parameters		Alendronate group		Chlorohexidine group		p-value@
		ALN with SRP (n=20) Mean±SD	SRP (n=20) Mean±SD	CHX with SRP (n=20) Mean±SD	SRP (n=20) Mean±SD	
Total bacterial count	Baseline	930.0±95.1	940.0±96.8	912.5±95.8	932.5±69.4	0.8
	After 3 months	405.0±126.6	490.0±94.0	417.5±120.0	470.0±147.3)	0.09
	p-value*	<0.001	<0.001	<0.001	<0.001	
Prevotella intermedia	Baseline	28.2±6.5	28.0±3.4	28.7±6.5	29.0±3.9	0.93
	After 3 months	16.2±3.8	19.3±4.8	17.0±6.7	20.0±5.4	0.07
	p-value*	<0.001	<0.001	<0.001	<0.001	
Porphyromonas gingivalis	Baseline	28.1±4.4	28.1±4.0	28.5±3.4	28.7±4.5	0.9
	After 3 months	15.7±3.4	17.8±4.9)	16.7±6.5	20.1±6.4	0.07
	p-value*	<0.001	<0.001	<0.001	<0.001	

@: One-Way ANOVA test between groups, *: paired T-test within each group baseline vs follow up, TBC: Total Bacterial Count

Discussion:

Appropriate therapy for patients with periodontitis varies considerably with the extent and pattern of attachment loss, local anatomical variations, type of periodontal disease, and therapeutic objectives. The primary objectives are to cease disease progression and to resolve inflammation¹².

Regarding our results, it has been showed that there was a significant difference in clinical and microbiological assessment for all groups when comparing pre-treatment measurements vs post-three months treatment measurements. While, there was no significant difference in both clinical and microbiological assessment after three months when comparing both treatment groups either alendronate after SRP or chlorohexidine after SRP.

The local application of ALN gel has a beneficial influence on tissue repair owing to its anti-osteolytic, anti-inflammatory, and antimicrobial properties¹³. ALN group patients showed statistically significant improvement compared to their pretreatment values. These results could be explained as bisphosphate influences physiochemical processes associated with calcification. It acts on tooth enamel to the thermodynamics of the calcium phases of calcium salts, controlling calcification and the formation of hydroxyapatite (HA), achieving the ultimate goal of preventing dental calculus¹⁴.

Our results are agreed by Chen et al. who found that ALN increases bone defect fill by 38.25%, reduced the PD by 2.29 mm and CAL by 1.92 mm¹⁵. Other studies performed by Akram et al. and Muniz et al. showed a statistically significant PD reduction, and CAL gain with ALN application^{16,17}. This was inconsistent with Sharma et al. who showed improved periodontal clinical parameters and PD reduction when ALN gel (1%) was used in periodontitis patients¹⁸.

On contrary, Storrer et al who performed a study stated that ALN resulted in reducing bone reabsorption in rats infected by P. gingivalis. They explained that P. gingivalis may have promoted a reversal action in the host response towards the anti-inflammatory and anti-resorptive properties of ALN¹⁹.

Subgingival placement of CHX gel is commonly used as an adjunct to SRP which is considered the gold standard for periodontal therapy²⁰. CHX Group patients showed a statistically significant improvement. This result is justified as it has a broad-spectrum antimicrobial activity and anti-inflammatory action, inhibiting bone loss and promoting the attachment of fibroblast to the root surface²¹.

Our findings agree with a study performed by Paolantonio et al. reported significantly lower TBCs compared to baseline values in a 3-month time-points²². Firkova and

Stamenov evaluated the clinical efficiency of locally delivered 1.5% CHX gel and concluded that its application as adjunctive therapy in moderate and severe chronic periodontitis leads to better results in comparison to SRP only²³. Similarly, Vaish et al. concluded that 1.5% CHX gel and 2.5 mg biodegradable CHX chip as an adjunct to SRP provided significant results in the management of chronic periodontitis as compared to SRP alone²⁴.

The non-surgical periodontal treatment is based on mechanical supra-and sub-gingival debridement supplemented by the administration of antibacterial and antiseptic adjuvants and professional oral hygiene instruction²⁵. Our results agreed with Wejden et al, who concluded that active non-surgical periodontal therapy resulted in success endpoint of PPD \leq 5mm²⁶. Besides, another study which was conducted by Jentsch et al, showed improvement in PD, CAL, and bleeding on probing, after SRP²⁷.

Conclusion:

Considering the clinical relevance, local application of both ALN gel tested in this study as well CHX gel are valid adjunctive therapy to SRP. ALN gel revealed a significant improvement in clinical indices in addition to the reduction of *P. gingivalis* and *P. intermedia*.

ETHICAL CONSIDERATION

The proposal of the study was approved by the Dental Research Ethics Committee, Faculty of Dentistry, Mansoura University (Reference number M.S.A09150620).

Author's contributions

U.M.S, B.H.M: designed the study, controlled all study procedures, wrote and edited the manuscript. M.A.D: wrote and analyzed the microbiological data. A.M.H: collected the clinical parameters and microbiological samples. All authors discussed the results and contributed to the final manuscript.

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