AL-AZHAR
Assiut Dental Journal

The Official Publication of The Faculty of Dental Medicine, Al-Azhar Assiut University, Egypt

AADJ, Vol. 1, No. 1, October (2018) — PP. 39:48

Anew Approach Using Natural Chitosan Gel in the Treatment of ChronicPriodontitis Patients. (Clinical, Radiographic and Biochemical Study)

Mahmoud E.S.[1], Edress M.F[2] *and* Hassan K. S. [3]

Codex : 06/1810

Aadj@azhar.edu.eg

ABSTRACT

Objectives: The use of chitosan gel may be considered as a new local chemotherapeutic material for treatment of chronic periodontitis patients. This study was directed to evaluate clinical, radiographic and biochemical effects of 1% chitosan gel in the treatment of chronic periodontitis patients.

Methods: 20 patients were divided into two groups. Group I: consisted of 30 sides received SRP with intrapocket application of 1% chitosan gel. Group II: consisted of 30 sides received SRP only. All patients were subjected to initial phase therapy and instructed for plaque control regimen. Then, evaluated clinically and radiographically at baseline, 3 and 6 months after treatment. The laboratory evaluation of alkaline phosphatase enzyme level was done at baseline, 3 and 6 months after the treatment. The data were collected, tabulated and statistically analyzed by SPSS (Statistical Package for Social Sciences).

***Results*:** The clinical parameters such as probing depth,clinical attachment level, plaque index and gingival index were recorded at baseline at 3 and 6 months. In all groups, highly statistically significant differences were showed in both groups at the different intervals when compared to the baseline. *Plaque index* between the two groups representing no statistical significant difference in group I when compared with group II at different intervals. *Gingival index* showa statistical significant difference in group I when compared with group II at 3 and 6 months**.** *Probing depth* show a statistical significant difference in group I when compared with group II at 3 months and no difference at 6 months**.** *The Clinical attachment level* show a highly statistical significant difference in group I when compared with group II at 3 and statistical significant difference in group I when compared with group II at 6 months**.**

Conclusions: Intrapocket application of chitosan gel 1% appeared to be effective adjunctive in treatment of mild to moderate chronic periodontitis**.**

KEYWORDS

Chitosan gel, periodontitis,plaque,gingival index,probing depth

1. Demonstrator of Oral Medicine, Periodontology, Diagnosis and Oral Radiology Faculty of Dental Medicine, AL-Azhar University, Assiut.
2. Assistant professor and head of Oral Medicine, Periodontology, Diagnosis and Oral Radiology Faculty of Dental Medicine, AL-Azhar University, Assiut.
3. Professor of Oral Medicine, Periodontology, Diagnosis and Oral Radiology, Dean Faculty of Dental Medicine, AL-Azhar University, Assiut.

INTRODUCTION

Periodontal diseases is an entity of infections that involve tooth supporting tissues (i.e, gingiva, periodontal ligament, root cementum and alveolar bone) Chronic periodontitis is a term used to describe an inflammatory process initiated by the plaque biofilm that leads to loss

of periodontal attachment to the root surface and adjacent alveolar bone which ultimately results in tooth loss. It can also defined as a chronic infection that results from the interaction of periodonto-pathogenic bacteria and host inflammatory immune responses[1]. Alkaline phosphatase is a membrane bound glycoprotein produced by many cells within the periodontium and gingival crevice.It is a lysosomal enzyme that is released into crevicularfluid during inflammatory process by degradation of polymorphonuclear leucocytes, host tissue injury and bacterial degradation. It is associated with inflammation and hence alteration in its levels in GCF indicate initiation and progression of periodontitis. [2]

Periodontal pocket elimination is one of the most important goals of chronic periodontitis (CP) treatment. Gram negative anaerobic bacteria are generally suggested as the primary cause of CP and mechanical procedure is the treatment approach, which is performed nonsurgically or surgically[3]

Conventional periodontal therapy has been targeted to altering the periodontal environment to become a less bacterial plaque retentive one. With increased acceptance of the role of specific periodontal pathogens in the etiology of periodontal disease, antimicrobial therapy has been established as an adjunct to the traditional mechanical form of therapy. Systemic antibiotics can penetrate soft tissues and may target invasive organisms. It can be used to treat multiple sites simultaneously. It may also affect reservoirs of the bacterial reinfection such as saliva, the tonsils, and the oral mucosa[4-9]. Extensive use of antibiotics in periodontal treatment could contribute substantially to the development of bacterial antimicrobial resistance[10-17]. Local delivery antimicrobials have the advantage over systemic therapy of possibly achieving higher concentrations of drug at the intended site of action using a lower dosage with an associated reduction in side and toxic effects[18-21]. A variety of methods to deliver antimicrobial agents into periodontal pockets have been introduced. They include pocket irrigation, application of drug-containing ointments and gels, and devices for sustained drug release[22]. Biodegradable delivery systems dissolve in the gingival crevice so that their removal after treatment is not required. It also avoid the possible undesirable effects of a nondegradable device left in periodontal pocket. Drug release occurs by dissolution and drug diffusion through the matrix. It is possible to retain a formulation on the periodontal hard and soft tissue surfaces and prolong the duration of retention with the bioadhesive delivery systems [23-25].

Chitosan is a natural polysaccharide processed from deacetylation of chitin, a derivative of the exoskeleton of arthropods such as crabs, prawns, and lobsters. It has antimicrobial, anti-inflammatory, wound healing, and mucoadhesive properties that suggest its effective use in local drug delivery systems[25-28]. Chitosan also has another favorable properties such as non-toxicity, biocompatibility, and biodegradability[29]. The present study was designed to evaluate the clinical efficacy of chitosan gel formulations as adjunct to scaling and root planingin treatment of chronic periodontitis patients.

METHODOLOGY

This study was designed as a randomized, controlled clinical trial and carried out on thirty patients of both sex with mild to moderate chronic periodontitis**.** All patients were selected from those attending at the out patient clinic, Oral Medicine and Periodontology Department, Faculty of Dental Medicine, Al-Azhar University, Assiut Branch.

All subjects were

1. Free from any systemic diseases
2. Should have ≥20 teeth and bilateral two or more interproximal sites with pocket depth not more than 6 mm and clinical attachment level (CAL) less than 5 mm.

3. Were non-smokers and cooperative.
4. Were not subjected to previous periodontal therapy during 6 months..

Patients were classified randomly into the following equal groups using online software numbers were concealed in closed envelopes.

Group 1: consisted of 30 sides with mild to moderate chronic periodontitis were received conventional periodontal treatment (scaling and root planing) followed by application of 1% chitosan gel.

Group 2: consisted of 30 sides with mild to moderate chronic periodontitis were received conventional periodontal treatment (scaling and root planing) alone.

Periodontal evaluation The periodontal conditions of each patient were evaluated at base line, 3 and 6 months after treatment using the following periodontal parameters:-Plaque Index (PI), Gingival Index (GI),Probing Depth (PD) and Clinical Attachment Level (CAL)[30-32]. .

Radiographic Evaluation

Radiographic assessment of the amount marginal bone level at base line, 3 and 6 months were done by an image analyzer .

For achieving standerazation: Bite registration block were made for each patient to adjust film position at different intervals .Radiographs were taken by parallel technique using film holder and photostimulated phosphorplate size 2.

Sample collection and preparation

- Gingival Crevicular Fluid (GCF) samples were obtained from the site which showed the highest probing depth (range 3-6 mm).
- The teeth selected for sampling were isolated with cotton roll, and supragingival plaque was removed without touching the marginal gingiva.
- The crevicular site was then dried gently with an air syringe.
- Samples of GCF were obtained before probing into the site by placing Sterilized paper point size# 30was carefully inserted to the maximum depth of the periodontal pocket and held in position for 30 seconds.
- The collected GCF was immediately transferred into an Eppendorf tube containing phosphate buffer saline.

1% Chitosan gel preparation:

The chitosan is dissolved in an acetic acid solution (pH = 4). The prepared solution is injected drop by drop using a syringe in agelling solution (solution of sodium hydroxide 3M or sodium dodecylsulphate solution 50mM). The obtained solution is maintained for 6 hours at room temperature (25°C). Obtained hydrogel (in the form of balls) is filtered, then immersed in baths containing ethanol/water solutions. One obtains finally an alcogel, which there after undergoes an evaporative drying or a drying with supercritical CO2 to finally obtain 1% concentration.

Periodontal treatment:

Following the initial examination, all patients received a course of basic periodontal treatment consisted of scaling, root planing and oral hygiene instructions.

Application of 1% chitosan gel:

Following the conventional periodontal treatment (scaling and root planing), intrapocket application of 1% chitosan gel was done to the patients of the first group (test group)Figure (1).

Statistical analysis:

The data were collected, tabulated and statistically analyzed.

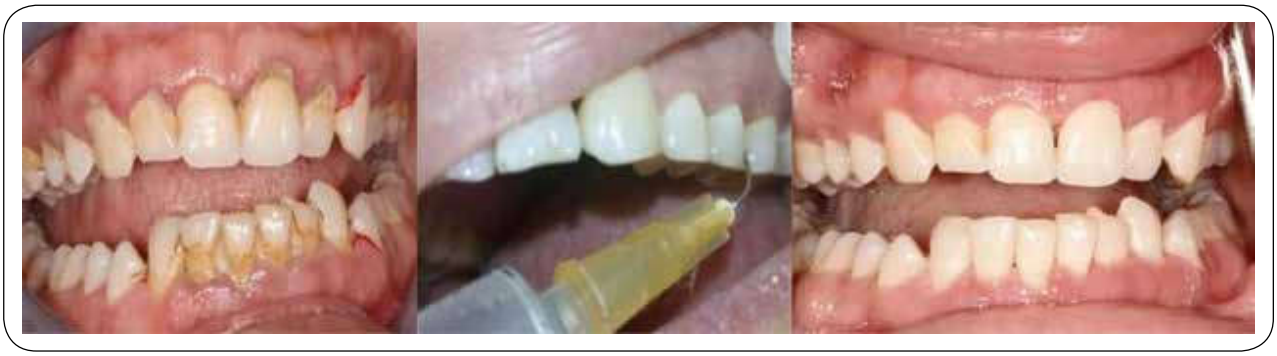

Fig. (1) A clinical photographs of female 29 aged patientbefore,duringand after treatment.

RESULTS

Changes in Plaque Index (PI):

The changes in PI scores during the observation periods of the present study for both groupstable (1). Paired t-test showing high statistically significant difference in both groups at the different intervals when compared to the baselineThe mean value of plaque index in group I was2.22 ± 0.22 at baseline that reduce to 0.84±0.08 after 6 months of the treatment (P=>0.001).The mean value of plaque index in group II was 2.18 ± 0.2 at baseline that reduce to 0.87± 0.11 after 6 months of the treatment (P=>0.001).unpaired t-test for comparing means ± standard deviations, between the two groups representing no statistical significant difference in group I when compared with group II at different intervals, table(2).

Changes in Gingival Index (GI)

The changes in GI scores during the observation periods of the present study for both groups. Paired t-test showing highly statistically significant difference in both groups at the different intervals when compared to the baseline.The mean value of gingival index in group I was 2.25±0.24 at baseline that reduced to 0.84 ± 0.1 after 6 months of treatment (P=>0.001).The mean value of gingival index in group II was 2.22±0.27 at baseline that reduce to 0.95 ± 0.13 after 6 months of treatment (P=>0.001)table(1).unpaired t-test for comparing means± standard deviations, between the two groups representing statistical significant difference in group I when compared with group II after3 and 6 months, table (2).

Probing Pocket Depth Measurements:

The changes in PPD measures in millimeter during the observation periods of the present study for both groups.Paired t-test showing highly statistically significant difference in both groups at the different intervals when compared to the baseline . The mean value of probing depth in group I was 4.39 ±0.42 at baseline that reduced to 2.89± 0.29 after 6months of the treatment (P=>0.001). The mean value of probing depth in group II was 4.32± 0.41 at baseline that reduced to 3.09± 0.39 after 6 months of the treatment (P=>0.001) table(1).Unpaired t-test for comparing means± standard deviations, between the two groups at different intervals representing statistical significant difference in group I when compared with group II at 3months while no significant difference in group I when compared with group II at 6 months.

Clinical Attachment Level Measurements:

The changes in CAL measures in millimeter during the observation periods of the present study for both groups.Paired t-test showing highly statistically significant difference in both groups at the different intervals when compared to the baseline. The mean value of CAL in group I was 3.18±0.51 at baseline that reduced to 2.05±0.31 after 6 months of the treatment (P=>0.001). The mean value of CAL in group II was 3.24±0.37 at baseline that reduced to 2.36± 0.42 after 6 months of

the treatment (P=>0.001)table(1).Unpaired t-test for comparing means± standard deviations, between the two groups representing highly statistical significant difference in group I when compared with group II at 3 and statistical significant difference in group I when compared with group I at 6 months, table(2).

Marginal bone Level Measurements

The changes in marginal bone Level measures in millimeter during the observation periods of the present studyfor both groups. Paired t-test showing highly statistically significant difference in both groups at the different intervals when compared to the baselin. The mean value of in group I was 3.23±0.29 at baseline that reduced to 2.05±0.36 after 6 months of the treatment (P=0.000). The mean value of CAL in group II was 3.14±0.38 at baseline that reduced to 2.23±0.35 after 6 months of the treatment (P=>0.001)table(1).Unpaired t-test for comparing means± standard deviations, between the two groups representing statistical significant difference in group I when compared with group II at 3 while no statistical significant at 6 months, table(2).

Changes in alkaline phosphatase (ALP) levels:

The changes in ALP level inpicogram level during the observation periods of the present study was for both groups. Paired t-test showing high significant difference in both groups at 3 months and 6 months when compared to the baseline. The mean value of ALP level in group I was 116.86±13.19 at baseline that decreased to 37.06 ± 10.59 after 6 months of the treatment(P=> 0.001).The mean value of ALP level in group II was 117.78 ± 13.91 at base line that decreased to 38.93 ± 6.90 after 6 months of the treatment (P=>0.001)table(1).Unpaired t-test for comparing means ± standard deviations, between the two groups representing that there is no statistically significance difference between the two groups when compared with each other at different evaluation periods, table(2).

Table (1): *Showing means±SD and Paired sample t- test of Plaque Index,gingival Index,Pocket depth, CAL, marginal bone level and ALP levels in both groups.*

Parameters	Period	Baseline	3 months	6 months	**3 months vs Baseline**		**6 months vs Baseline**	
		Mean	Mean	Mean	**Paired sample t- test**			
	Group	±SD	±SD	±SD	**T**	**P**	**t**	**P**
Plaque Index	**Test**	2.22±0.22	0.82±0.09	0.84±0.08	29.185	<0.001**	26.473	<0.001**
	Control	2.18±0.2	0.84±0.09	0.87±0.11	32.927	<0.001**	29.148	<0.001**
gingival Index	**Test**	2.25±0.24	0.89±0.08	0.84±0.1	25.372	<0.001**	22.683	<0.001**
	Control	2.22±0.27	1±0.14	0.95±0.13	22.277	<0.001**	22.624	<0.001**
Pocket Depth	**Test**	4.39±0.42	3.35±0.34	2.89±0.29	12.943	<0.001**	16.164	<0.001**
	Control	4.32±0.41	3.67±0.36	3.09±0.39	11.599	<0.001**	20.791	<0.001**
CAL	**Test**	3.18±0.51	2.41±0.37	2.05±0.31	10.321	<0.001**	11.714	<0.001**
	Control	3.24±0.37	2.8±0.36	2.36±0.42	6.928	<0.001**	9.838	<0.001**
marginal bone level	**Test**	3.23±0.29	2.41±0.36	2.05±0.36	14.589	<0.001**	17.824	<0.001**
	Control	3.14±0.38	2.74±0.39	2.23±0.35	5.678	<0.001**	10.280	<0.001**
ALP levels	**Test**	116.86±13.19	73.07±14.53	37.06±10.59	10.210	<0.001**	20.462	<0.001**
	Control	117.78±13.91	72.53±15.09	38.93±6.90	9.688	<0.001**	16.536	<0.001**

Table (2): *Showing Unpaired sample t-test of Plaque Index,gingival Index,Pocket depth, CAL, marginal bone level and ALP levels in both groups.*

Parameters	Unpaired t- test						
	Period	Baseline		3 months		6 months	
		T	P	T	P	T	P
Plaque Index	G1 vs G2	0.524	0.604	0.392	0.698	0.777	0.444
gingival Index	G1 vs G2	0.412	0.683	2.678	0.012*	2.747	0.010*
Pocket depth	G1 vs G2	0.511	0.613	2.487	0.019*	1.612	0.118
CAL	G1 vs G2	0.370	0.714	2.944	0.006**	2.325	0.028*
marginal bone level	G1 vs G2	0.680	0.502	2.387	0.024*	1.371	0.181
ALP levels	G1 vs G2	0.185	0.854	0.101	0.921	0.571	0.367

Statistically significant: ($p < 0.05$).* *: High statistically significant: ($p < 0.01$)*

DISCUSSION

In the present investigation chronic periodontitis patients were selected because this condition is considered as one of the most common bacterial infection worldwide with prevalence in mild to moderate forms ranging from 13% to 57% in different populations depending on oral hygiene and socio-economic status[33,34].

The primary goals of the periodontal therapy are to preserve the natural dentition, to maintain and improve periodontal health, comfort, esthetics and function. As regard to the conventional strategies for treatment of chronic periodontitis by effective plaque control and calculus removal as well as regular follow-up combines with oral hygiene instruction can significantly enhance the clinical parameters and reduce the clinical signs of inflammation. About 20%–30% of all chronic periodontitis cases do not respond favorably to conventional periodontal treatment. Many factors may contribute to that response, such as improper removal of bacterial deposits and calculus, poor plaque control, systemic conditions leading to an impaired immune response, defective restorations, occlusal dysfunction, periodontal-endodontic involvement and others. In these cases, other treatment approaches may be required [35].

Application of local drug delivery as adjunctive to scaling and root planing provide a sustained release of short doses of the drug over a long period of time without need to dose repeatedly unlike systemic antibiotics and sub gingival irrigation[36]. In addition, it was reported that, the use of these local delivery drugs reduce probing depth, sub gingival microflora and clinical signs of inflammation. [37,38].

The present study aimed to use a new modality in the periodontal therapy by intrapocket application of chitosan gel 1% as adjunctive to the basic conventional therapy to overcome the unresponsive cases treated by conventional periodontal therapy alone. Because of its ability in impairing the colonization of the tooth surface by Streptococcus mutans, chitosan has been shown to be potential in minor quantities in toothpastes, mouth-rinses, or chewing gum[39]. In addition, it possesses bioactive properties including wound healing, antimicrobial, tissue regeneration, and hemostatic activities[40] .

Plaque index scores recorded in the results of this study showed highly statically significant

difference in both groups at the different intervals when compared to baseline, while no statically significant difference in group I when compared with group II. Similarly,the results of gingival index showed highly statically significant difference at the different intervals as compared to baseline, while in group I it was statistically significance difference when compared with group II at 6 months. This is in agreement to the findings of Akncbay H(2007) [41]. This could be attributed to patients cooperation and motivation during the observation period of the study and to the anti-inflammatory effect of chitosan.

In the present study the probing pocket depth measurement showed a highly statically significant difference in group I and group II at 3 and 6 months when compared to baseline, while there was no statically significant difference in group I when compared with group II at 6 months. These results are in accordance to the findings of Akncbay H (2007)[41]. However the mean difference of probing pocket depth in group I when compared with group II at 3 months was statistically significant difference, These results are in contrary to the findings of Akncbay H (2007) [41]who recorded that statistically significant difference between two groups at 3 and 6 months. This may be attributed to the difference of number and frequency of application of chitosan according to Akncbay H, injection repeated twice weekly for 6 months, but in this study injection repeated weekly for 3 months.Reduction in PPD is a beneficial clinical outcome used to assess the success of periodontal therapy, it can be conjectured that the anti-bacterial properties of chitosan aided in decreasing the PPD.

The gain in clinical attachment level at 6 months showed a highly statistically significant difference in group I and group II whstatistically en compared to baseline. In addition, the gain in clinical attachment was highly statically significant greater in group I when compared to group II at 3 months and statistically significant at 6 months. These results in contrary to study ofAkncbayH(2007) [41] who showed no significant gain in clinical attachment level in chitosan treated patients. Chitosan is a bioadhesive and the reduction in PD values and the gain in clinical attachment level could be the result of the attachment on the root surfaces which could be allowed by chitosan because of its supportive and organizing effect on the histological architecture of the gingiva. However, the type of the attachment after chitosan application and soft tissue healing should have defined with histological investigations in future studies[42]. A change of the marginal bone level was detected radiographicaly and aserial radiograph should be staderdized by using bite registration block to minimize the measurement errors.

The results of the present study showed asignificant decrease in marginal bone loss in group 1 on comparing both groups at 3 months. This is similar to the findings of DuyguBoynueg˘ri et al (2009) [42], They evaluated the uses of 1% chitosan gel alone for treatment of periodontal defects and reported a favorable bone fill. Moreover Yeo et al (2005) [43]reported that chitosan effectively contributed to the formation of new bone and cementum in surgically created one-wall intrabony defects in beagle dogs . These properties make it a promising material in the guided tissue regeneration and guided bone regeneration (GTR/GBR). However, no statistically significant difference of the marginal bone level in group I when compared with group II at 6 months, this could be attributed to decrease cooperation and motivation of the patients at the end the observation period of the study.

With reference to the GCF ALP levels in the present study, there was a marked decrease with highly statistically significant difference in both groups at the different intervals when compared to the baseline. While by comparing the two groups, there was no statistically significance difference in group I when compared with group II. This is in agreement with the finding of DurgaBaiYendluri, Aditi R (2016)[45] they measured elevated levels of ALP in diseased sites and low levels of ALP in all the

treated sites.Clinically, periodontitis patients under chitosan therapy had less number of pathological periodontal pockets compared with those without under chitosan medication. Improvement in the clinical parameters was observed following scaling and root planing with locally delivered chitosan in periodontitis patients, compared with scaling and root planing only [42]

CONCLUSIONS

- Intrapocket application of chitosan gel 1% appeared to be attractive and effective adjunctive in treatment of mild to moderate chronic periodontitis.
- Alkaline phosphatase enzyme is a good laboratory marker to determine periodontal disease activity and also to evaluate the treatment outcoms.
- Further long term clinical trials and histometric studies are needed for ratify the outcomes of this study, and to clarify the beneficial effects of chitosan gel 1% in treating periodontal diseases.

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