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Clinical Assessment of Potential Role of Chitosan in The Management of Periodontitis Patients

Hatem Mohamed Abd Alaziz[1], Nadia Fathy Hassabou [2], Amany Ahmed Al Araby[3], Hala Hassan Yassin [4], Hala Kamal [5]

1. MSc Periodontology, Faculty of Dentistry, October 6 University, Giza, Egypt. E-mail: 202100122@o6u.edu.eg ORCID NO. 0009-0004-7212-1001
2. Associate Professor of Oral and Maxillofacial Pathology, Faculty of Dentistry, October 6 University, Giza, Egypt. E-mail: nadiahassabou.dent@o6u.edu.eg ORCID NO. 0000-0003-4540-43859
3. Lecturer of Oral Medicine, Periodontology and Oral Radiology, Faculty of Dentistry, October 6 University, Giza, Egypt. E-mail: AmanyAhmed.dent@o6u.edu.eg ORCID NO. 0000-0002-6370-8693
4. Professor of Oral Medicine, Periodontology, Oral Diagnosis and Radiology, Faculty of Dentistry, Arab Academy for Sciences and Technology and Maritime Transport, New-Alamein, Alexandria. E-mail: halayassin118@hotmail.com
5. Professor of Oral Medicine and Periodontology, Faculty of Dentistry, Ain Shams University. E-mail: dr.halakamal@hotmail.com

Corresponding author*:

Hatem Mohamed Abd Alaziz, E-mail: 202100122@o6u.edu.eg

Periodontology Department, Faculty of Dentistry, October 6 University, Giza, Egypt.

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ABSTRACT

Aim: The use of chitosan gel may be considered as a new local chemotherapeutic material for the treatment of chronic periodontitis patients. This study aimed to evaluate the clinical effects of 1 % chitosan gel in treating intrabony defects in periodontitis. **Materials and Methods:** 30 patients were allocated into two distinct cohorts. Group I comprised 15 participants who underwent scaling, root planning, and intrapocket administration of chitosan gel. The Control Group encompassed 15 individuals who received scaling and root planning. Subsequently, all subjects underwent the initial phase of therapy and were educated on a regimen for controlling plaque. They were then assessed clinically at baseline, as well as at 3- and 6-months post-treatment. **Results:** Clinical parameters, including probing depth and clinical attachment level, were documented at baseline, 3 months, and 6 months. Significant statistical variances were observed within each group across the different time points in comparison to the baseline measurements. Particularly, probing depth exhibited a notable difference in Group I compared to Group II at the 3-month mark. Regarding clinical attachment level, Group I displayed a significant contrast with Group II at the 3-month interval, and a comparable distinction was noted between the two groups at the 6-month evaluation.

Conclusions: Intrapocket application of chitosan gel 1 % appeared to be effective adjunctive in the treatment of stage II to III chronic periodontitis.

Clinical Relevance: Topical application of chitosan gel provides a pivotal role in the treatment of periodontitis.

Keywords: Chitosan gel, Chronic periodontitis, Clinical attachment level, Pocket depth.

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1. Introduction

Periodontitis is characterized as a persistent inflammatory condition of the oral cavity induced by bacterial biofilm adhering to tooth surfaces, leading to degradation of the periodontal tissues through the interplay between periodontopathogenic microorganisms and the immune response of the host, where the periodontal pathogenic microorganisms initiate the disease progression [1].

The primary objective of periodontal treatment is to enhance the gum health of the individual and safeguard the existing periodontal tissues. Reduction of both local factors and the bacterial presence of periodontopathogens is essential, along with addressing behavioral aspects such as discontinuation of smoking and tobacco use as components of periodontal therapy [2].

Chitosan, a positively charged polysaccharide, is naturally present or produced by the deacetylation process of chitin, exhibiting a linear configuration consisting of Beta-1, 4O-glycosylamine. The active sites of chitosan involve amino and amide groups located at the C-2 position, along with hydroxyl groups at C-3 and C-6. The enzymatic hydrolysis-assisted deacetylation mechanism transforms chitosan into a soluble in water, oligosaccharide with low molecular weight. Through its ability to dissolve in weakly acidic solutions, chitosan creates a positively charged polymer, showcasing compatibility with living organisms characterized by its high viscosity and capacity to bind with water, making it appropriate for diverse applications such as gels, chips, and membranes. [3,4].

Moreover, chitosan, a hydrophilic polysaccharide, provides a wide range of bio-dental applications owing to its antimicrobial, immunostimulatory, hemostatic, and wound-healing characteristics. Within the realm of pediatric dentistry, chitosan is employed to inhibit the attachment of cariogenic bacteria to mucosal surfaces. [5]. Its incorporation in chewing gum and mouthwash is attributed to its antibacterial and antiplaque effects [6].

Chitosan's antimicrobial properties help prevent infections, thanks to its derivatives that include functional groups such as quaternary ammoniumyl, guanidinyl, carboxyalkyl, hydroxyalkyl, thiol-containing groups, and hydrophobic groups. These hydrophobic groups can consist of long alkyl chains, as well as substituted phenyl and benzyl rings [7].

It has been postulated that the protonation of amino groups of chitosan in contact with physiological fluids is a widely held belief. The interaction of chitosan with anionic groups of microorganisms leads to the agglutination of microbial cells and the inhibition of their growth. Furthermore, the antimicrobial properties of chitosan are closely linked to the absorption of polysaccharides by bacteria, resulting in modifications to the cell wall structure and increased permeability of the cell membrane, ultimately leading to cell death. Additionally, chitosan has been noted to disrupt bacterial coaggregation [8]. It has demonstrated that formulations containing chitosan exhibit prolonged retention at the site of application. Its capacity for tissue regeneration and hemostatic characteristics obviate the need for additional materials like barrier membranes and bone grafts in regenerative treatments. Furthermore, chitosan displays osteoconductive properties and promotes neovascularization, thereby facilitating accelerated bone growth [9].

The biodegradability and biocompatibility of chitosan make it a suitable option for utilization as a biomaterial and scaffold in the context of hard tissue regeneration. Due to its chemical composition featuring hydrogen bond chains, cross-linkages, and its interaction with negatively charged tissues within the human

body, chitosan establishes a steady setting that is conducive to the initiation of new bone cell generation in the initial phases of bone repair. There is substantial evidence endorsing the idea that the porous nature of chitosan fosters the proliferation of osteoblasts, boosts osteogenesis, and plays a role in guided bone regeneration [10]. Chitosan has been observed to influence specific cells crucial to the wound healing process, stimulating macrophages to release IL-1, which in turn promotes fibroblast proliferation [11].

In separate investigations, it was discovered that a 3% concentration of chitosan could serve as a suitable base for optimizing drug dosage and enhancing drug efficacy as a local delivery agent. Furthermore, a local drug delivery system utilizing chlorhexidine with a chitosan base polymer resulted in reduced probing depths and increased clinical attachment levels. The findings suggest that chitosan-loaded drugs could represent a viable treatment option for patients with (CP)during recall visits [12]. Additionally, chitosan finds application in various drug delivery contexts, spanning from oral drug administration to systemic therapy for diverse purposes such as insulin delivery, anticancer treatments, and gene therapy [13]. The present work aimed to assess the potential role of chitosan in the management of periodontitis patients.

2. Materials and Methods

2.1 Patient selection:

The current study incorporated 30 individuals diagnosed with stage II to III periodontitis. Allocation of patients into two groups was done randomly. Participants were chosen from the outpatient facility of the Oral Medicine and Periodontology Department within the Faculty of Dentistry. The screening process of patients was carried out until the desired parameters were met. Approval for this research was obtained from the ethics committee associated with the academic Faculty of Dentistry following the Helsinki Declaration. All participants in this research study provided written consent and expressed full willingness to take part in the research endeavor.

2.2 Inclusion and Exclusion criteria:

Inclusion criteria:

Patients were selected to be systemically free "according to the modified Cornell Medical Index". Patients having stage II to III periodontitis with probing pocket depths ≥ 5 mm, interdental CAL 3-4mm to ≥ 5mm [14].

Exclusion criteria:

Patients received antibiotics, anti-inflammatory, and periodontal procedures within the previous 6 months preceding the study. Smokers' patients. Participants complying with the inclusion criteria were randomly assigned using a computer-generated list of random numbers" [15].

2.3 Preparation of materials:

Chitosan was purchased with low molecular weight (50.000 to 100.000 u) and degree of de-acetylation (DD 75 %).

1) The chitosan is solubilized within a solution of acetic acid (with a pH of 4). The solution that is prepared is slowly administered using a syringe into a gelling solution (comprising either a 3M sodium hydroxide solution or a 50 mM solution of sodium dodecyl sulfate). The resulting solution is left undisturbed for 6 hours at ambient temperature (25°C).
2) The hydrogel that is obtained (presented in the shape of spheres) is sieved and then submerged in reservoirs containing solutions of ethanol and water. Subsequently, an

alcogel is produced, which then proceeds to endure either evaporation-induced drying or supercritical CO2 drying to ultimately achieve a concentration of 1%.

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

2.4 Study groups:

The patients were divided equally into two groups as follows:

- **Group I -n=15 (Chitosan hydrogel):**

  The periodontal pockets ≥ 5mm were isolated. Chitosan hydrogel was prepared in the same steps that mentioned before in the methodology and then the prepared gel was applied to the site of the defect with the deepest probing pocket measurement twice per week for one month [16]. Periodontal dressing (Coe-pack) was to secure the hydrogel in place.

- **Group II -n=15 (Control group):**

In the control group, patients were treated with scaling and root planning only and full periodontal charts were obtained.

2.5 Clinical Parameters Assessment

The following clinical parameters were evaluated for every patient included in the study at baseline, 3, and 6 months after treatment **(Fig. 1 A & B):**

- Periodontal probing depth (PD) according to Glavind and Löe (1967) [15].
- Clinical attachment level (CAL) [16].

2.6 Statistical Analysis

All assessed parameters were statistically analyzed with SPSS-16 statistical software. First data All data were presented as mean and standard deviation. Student t-test was used to evaluate the difference between the two groups. One–way analysis of variances (ANOVA) was used to analyze the data for several groups. "P-value was considered significant when $P \leq 0.05$".

3. Results

The current study involved a cohort of 30 individuals diagnosed with stage II to III periodontitis. The participants were allocated randomly into two equivalent cohorts.

The oral health condition of all subjects enrolled in this research was evaluated based on PD, and CAL at the beginning, three months, and six months, respectively. The information obtained from all participants examined in this study was documented, organized into tables, and analyzed statistically, with results presented as mean and standard deviation.

3.1 Probing depth (PD) measurement

By comparing the PD at baseline (0 months) between the treated and control group it was revealed that the difference in PD was statistically Non-significant with a P-value of 0.1, a Significant difference with a P-value of 0.03 at 3 months, and highly significant values 0.00001 at 6 months were observed. Highly significant values were revealed by comparing studied groups at different durations **(Tables 1,2), Fig (2 A**).

3.2 Clinical attachment loss (CAL) measurement

The same values of PD were observed in CAL measurement because all cases were without recission or enlargement of the gingiva, **Table (1,2), Fig (2 B).**

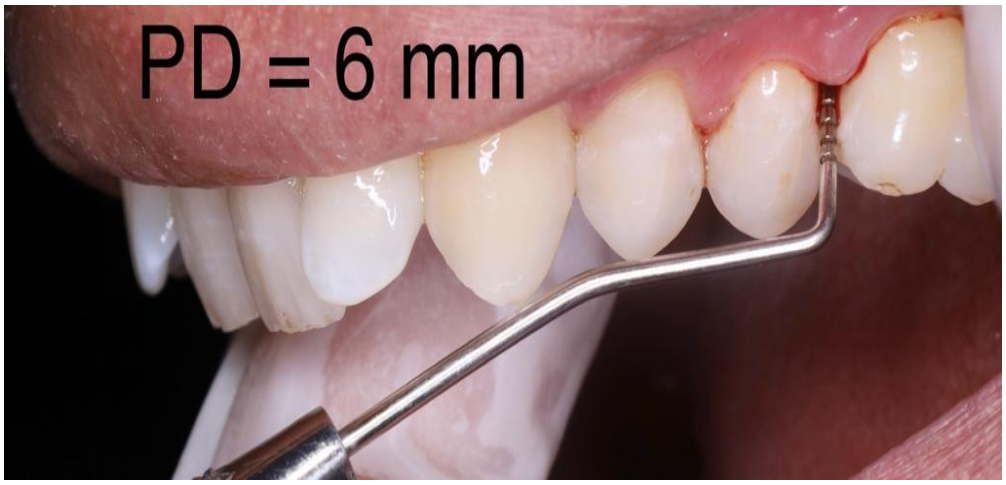

Fig. (1): Measurement of PD before treatment

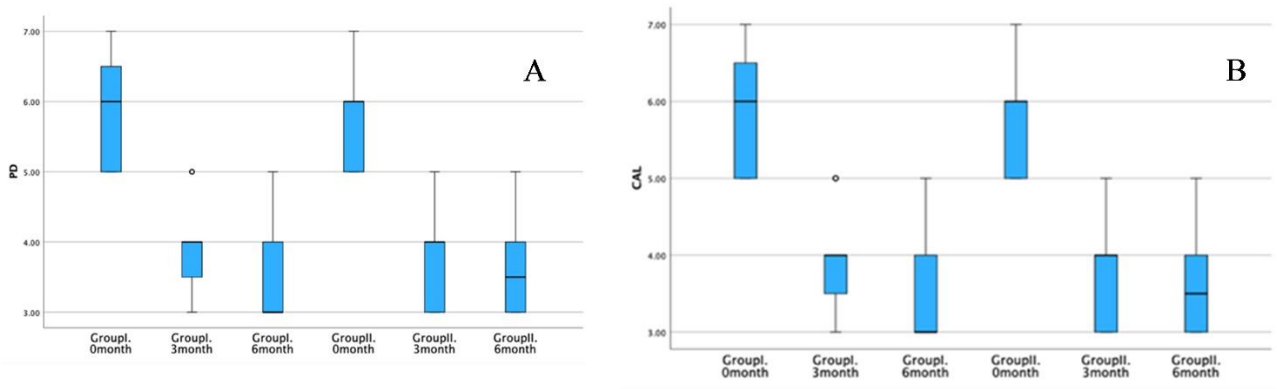

Fig. (2): PD and CAL of chitosan and control group

Table (1): Mean values and measures of viability (SD) for PD and CAL of chitosan and control group at different durations utilizing One-way ANOVA test.

Studied Groups	m±SD			f-ratio	P-value
	Baseline	3 Months	6 Months		
G1(Chitosan Group)	5.31±0.63	2.98±0.63	3.37±0.58	142.35	0.00001*
G2 (Control Group)	5.12±0.68	3.21±0.58	4.93±0.58	66.37	0.00001*

Table (2): Mean values for PD and CAL of chitosan and control group at different durations utilizing Student t-test.

	Baseline		3 Months		6 Months	
Studied Groups	G1	G2	G1	G2	G1	G2
Mean Value	5.31	5.12	2.98	3.21	3.37	4.93
T-Value	1.29635		-2.02925		-8.64957	
P-Value	0.1		0.03		0.00001	

4. Discussion

The investigation at hand focused on the selection of (CP)patients due to their status as a prevalent bacterial infection worldwide, with a prevalence ranging from 13% to 57% in different populations, depending on oral hygiene and socio-economic status [17].

The main objectives of periodontal therapy include the preservation of natural dentition, and the enhancement of periodontal health, comfort, esthetics, and function. Traditional strategies for treating (CP)involve effective plaque control, calculus removal, regular follow-up, and oral hygiene instructions, which collectively lead to improved clinical parameters and reduced signs of inflammation. However, 20%–30% of (CP)cases do not respond well to conventional treatment due to various factors such as inadequate bacterial deposit removal, poor plaque control, systemic conditions affecting immune response, faulty restorations, occlusal issues, and periodontal-endodontic complications, necessitating alternative treatment approaches [18-19].

The utilization of local drug delivery as an adjunct to scaling and root planing enables the sustained release of the drug in short doses over an extended period, eliminating the need for repetitive dosing as seen with systemic antibiotics and subgingival irrigation. Moreover, studies have shown that local delivery drugs can decrease probing depth, subgingival microflora, and clinical signs of inflammation [20].

This study introduces a novel approach to periodontal therapy by incorporating the intrapocket application of 1% chitosan gel as an adjunct to conventional therapy to address cases unresponsive to conventional periodontal treatment alone [21,22]. Chitosan, known for its ability to hinder *Streptococcus mutans* colonization on tooth surfaces, has demonstrated potential for incorporation in toothpastes, mouth rinses, and chewing gum in small quantities [23]. The possession of bioactive properties, such as wound healing, antimicrobial effects, tissue regeneration, and hemostatic activities, is observed in addition to others [24].

The analysis of probing pocket depth measurements in the current research displayed a significant disparity between group I and group II at the 3-month mark compared to the baseline; however, a highly significant difference was noted between group I and group II at 6 months. These outcomes align with Akncbay H's (2007) research findings. Nonetheless, a noteworthy statistical variance in probing pocket depth between group I and group II at 3 months was detected, contrary to Akncbay H's (2007) [25] findings, which reported a significant difference between the two groups at both 3 and 6 months. This discrepancy could be attributed to variations in the number and frequency of chitosan applications. Akncbay H advocated for biweekly

injections over 6 months, while this study administered biweekly injections for just one month. The reduction in probing pocket depth is a positive clinical indicator for assessing the effectiveness of periodontal therapy, suggesting that chitosan's antibacterial properties may have contributed to this outcome.

A statistically significant increase in clinical attachment level at 6 months was evident when compared to the baseline in both group I and group II. Moreover, the enhancement in clinical attachment level was significantly higher in group I at both 3 and 6 months compared to group II. These results contradict Akncbay H's (2007) study, which did not show a notable improvement in clinical attachment levels among chitosan-treated patients. The bioadhesive nature of chitosan may explain the reduction in probing depth values and the increase in clinical attachment level, possibly due to its ability to attach to root surfaces and influence the histological structure of the gingiva. Nevertheless, future studies should include histological examinations to determine the type of attachment post chitosan application and soft tissue healing [26].

5. Conclusion

Intrapocket application of chitosan gel 1% appeared to be attractive and effective adjunctive in the treatment of stage II to III chronic periodontitis.

Declarations

Conflict of Interest

All authors declare that they have no conflict of interest.

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Ethics approval

The study protocol was approved by the Research Ethics Committee at the Faculty of Dentistry, October 6 University, Giza, Egypt. The principles of the Helsinki Declaration were followed in the conduct of the study.

Consent to Participate

Written informed consent was received from all participants involved in the study explaining the entire procedures

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