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## Clinical And Radiographic Evaluation of periodontal Infrabony Defects Treated With chitosan In Periodontitis Patients

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## Clinical And Radiographic Evaluation of periodontal Infrabony Defects Treated With chitosan In Periodontitis Patients

### Abstract

Chitosan is a naturally derived polymer that has been investigated for its uses as a biomaterial for drug delivery and anti-inflammatory. Recently, chitosan applications in bone regeneration has gained distinct interest. The aim of this study was to. evaluate clinically and radiographically the healing of the periodontal infra-bony defects using chitosan gel in periodontitis patients .Material & methods: Twenty periodontitis patients with bilateral infrabony defects having stage II and Stage III periodontitis were selected according to the criteria of AAP (2017) classification system of periodontal diseases and conditions. Using split mouth design, 20 defects were treated using chitosan gel; while contra-lateral defects were treated by flap only. A total of 40 periodontal infra-bony defects. were randomly assigned for treatment. The clinical parameters included clinical probing pocket depths and clinical attachment levels. Standardized periapical radiographs were recorded at baseline and 6 months after surgery. Results: The results were statistically analyzed and clinical and radiographic data. revealed a statistically significant difference between Chitosan and control sites in the parameters investigated with a significant bone fills versus baseline measurements ( $P < 0.05$ ).Conclusion: Chitosan gel showed promising benefit in the periodontal regeneration context among periodontitis patients.

### Keywords

Chitosan, Periodontitis, Infra bony defects

## 1. INTRODUCTION

Innovative approaches for the management of periodontal bone loss are being developed; chitosan become a potential new target for periodontal therapy. (Bartold, Cantley, & Haynes, 2010). Chitosan is a hydrophilic biopolymer acquired by alkaline deacetylation of chitin. It is major component of arthropod shells, and has been declared as bioadhesive and permeabilizer. Chitosan advantages include nontoxic, biocompatible, and biodegradable. Chitosan attract attention in various dental specialties due to antimicrobial activity; wound healing enhancement, hemostatic, and tissue regeneration properties. (Aksungura et al., 2004; Boynueğri et al., 2009)

Because of its bioadhesive and antimicrobial properties, chitosan containing formulations may remain for long-lasting time and also prevent any Possible infection after periodontal surgery. (Cicciù et al., 2019; Matarese et al., 2017)

Its tissue regeneration ability and hemostatic properties also eliminate any need for additional material. This enable dentists to spend less time in operations and offer more economical treatment modality for the patient. (Pippi et al., 2017) Advantages of chitosan include its self-adhesive nature and ability to be placed even on actively bleeding surface even in patients with bleeding disorders. It prevents wound from getting exposed to outside environment with residual acetic acid release was proved to reduce pain.(Boynueğri et al., 2009; G İkincia et al., 2002; Shen et al., 2006; Shin et al., 2005)

According to clinical studies, chitosan can be provided on a variety of methods where ideally 6 months follow up after the baseline treatment as well as 3 month period maintenance post-operatively is required to show significant improved bone behaviour on the tested oral areas, where decreased tissue inflammation and bleeding by probing (BOP) can be observed clinically as radiographic attachment levels can be enhanced concurrently. (Wohlfahrt, Aass, & Koldslund, 2019) To our knowledge, limited number of researches has evaluated clinically and radiographically chitosan gel application in the treatment of periodontitis.

### 1.1 The Aim of Study

This study aimed to evaluate clinically and radiographically the healing of the periodontal infra-bony defects using chitosan gel in periodontitis patients.

## 2. MATERIALS AND METHODS

Twenty periodontitis patients with bilateral infra-bony defects were enrolled in the study from the Periodontology clinic at the Faculty of Dentistry, BAU. The study was approved by the Institutional Review Board at Beirut Arab University- Lebanon with IRB Number 2019H-0071-HS-M-00315 patients signed a consent form indicating acceptance to join the study after discussing the benefits, risks, and alternative treatment modalities.

Exclusion criteria include: Pregnancy or during lactation period, allergy to Chitosan, intake of antibiotics or anti-inflammatory drugs 6 months prior treatment, smokers' patients, history of periodontal therapy 3 months before the treatment and history of any systemic diseases that would affect bone healing.

These patients were chosen according to the criteria of the American Academy of Periodontology (2017) (Papapanou et al., 2018) and included periodontitis patients having moderate to advanced loss of periodontal tissue with bilateral infra-bony defects .

### 2.1 Clinical Parameters

Forty periodontal infra-bony defects were randomly treated using split mouth design, 20 defects were treated in each patient using chitosan gel; while contra-lateral control sites defects were treated by flap only. Clinical probing pocket depths, clinical attachment level. In addition to, standardized periapical x-rays were taken at baseline and 6 months after surgery.

### 2.2 Radiographic Evaluation

Standardized periapical radiographs were taken to the teeth included in the study before treatment procedures and 6 months after the surgery. An individual silicon bite stent and a film holder device, in which the X-ray tube-fitted were used with the purpose of standardization.

Radiographic infra-bony defect depth were represented by calculating the distance between the (CEJ) and the bottom of the bone defect in a line parallel to the long axis of the tooth immediately adjacent to the proximal location being measured.(Boynueğri et al., 2009)

### 2.3 Preparation of the (10%) Chitosan Gel

A solvent was formed by mixing 1% glacial acetic acid solution and glycerol in a ratio of 1 part of acetic acid solution to 3 parts of glycerol. Then, one gram of fine powder chitosan was dissolved in 100 ml of the aforesaid solvent by stirring for one to two hours with a magnetic stirrer at room temperature. The formed clear pale yellow solution was neutralized by adding 5N NaOH until pH 7 was reached. Instantly, a clear slightly tacky gel formed as a result of the ingredient interaction of chitosan, glycerol and water. The gel has a three dimensional structure, and no free water or glycerol is apparent.(Boynueğri et al., 2009)

### 2.4 Treatment procedures

All patients received complete dental examination including medical and dental history, full mouth periodontal charting, and comprehensive treatment plan. Prior to surgical procedures, patients were recalled at weekly interval to receive optimum oral hygiene including deep gingival scaling and root planning using hand and ultrasonic instruments, rubber cup polishing and oral hygiene instructions. After initial therapy completion, the patients were re-evaluated to review the criteria for surgery. Surgical procedures were carried out under local anesthesia. After raising the periodontal flap, debridement & root planning were done with hand instruments, the defects were rinsed with sterile saline. Chitosan were added without overfilling the defect. Finally the flaps were repositioned coronally and closed with 4/0 silk mattress sutures.(**Figures 1-6**) The contra-lateral defects similarly were surgically treated but without the application of Chitosan.



Fig.1: Periapical x-ray showing upper poster right segment with infrabony defect related to the first molar



Fig.2: Preoperative picture, showing the calibrated periodontal prob measuring 7 mm probing pocket infrabony defect



Fig.3: During periodontal surgery, showing flap reflection with infrabony defect in the mesial surface of upper first molar



Fig.4: Chitosan gel application in the infrabony defect



Fig.5: Bony defect filled with chitosan gel



Fig.6: Flap repositioned coronally and closed with 4/0 silk suture

### 2.5 Postoperative Care

Prescription of (amoxicillin 500 mg, t.i.d.) for 1 week after surgery and .2% chlorhexidine mouth rinse twice daily for two weeks was given the patient. The suture removal was done after 7–10 days. Scheduled appointments were every second week for 2 months after surgery. And once a month up to four months for clinical and radiographic reevaluation (**Figures 7 and 8**).

### 2.6 Statistical Analysis

Data were analyzed using SPSS Statistics software, version 23.0.0. Variations in the clinical and radiographic parameters investigated over time were assessed using repeated-measures analysis of variance. Intragroup comparisons at 6 months, versus baseline measurements were conducted using the paired t-test. Intergroup comparisons of parameters change investigated compared to baseline were performed using Student's t-test. The significance level was set at  $P < .05$ .

## 3. RESULTS

Twenty periodontitis patients (15 females and five males) participated in the study. Their age ranged from 33 to 49 years. They had at least ten sites with more than five mm of clinical attachment loss on at least two teeth per quadrant as well as radiographic evidence of bone loss of more than one-third of the root length. Two contra-lateral periodontal infra-bony defects, with probing depths more than six mm and radiographic evidence of bone loss of at least three mm. A total of 40 infra-bony defects were treated. No inflammatory reactions were observed following the application of chitosan gel during maintenance visits.

Table 1 shows the clinical probing depth of the Chitosan sites and Control sites at various time.

At baseline, there was no statistical significant difference between chitosan and control sites regarding the mean and SD of both clinical probing depths and attachment levels ( $P > 0.05$ ). At 6 months both sites showed significant improvement in clinical parameters over baseline values. Statistically significant difference when the two sites where compared ( $P < 0.05$ ).

Table 1: The clinical parameters of the Chitosan sites versus control sites at time intervals

Clinical parameters	Baseline	Chitosan sites		Control sites	
		Baseline	At 6 months	Baseline	At 6 months
Clinical probing depth	Range	6–10	3–5	6–10	4–6
	Mean± SD	8.48±0.5*	3.9±0.7**	8.83±0.34	5.1±0.8
Clinical attachment level	Range	6–9	4–6	6–9	5–7
	Mean± SD	7.21±0.35*	4.85±0.65**	7.75±0.96	5.78±0.88

Chitosan sites versus Control sites at: \*Baseline, not significant \*\*six months, P<0.05 significant

Table 2 shows the radiographic infra-bony defects depth of the Chitosan sites and the control sites at various time intervals. At baseline, regarding the radiological depth of infra-bony defects there was no statistical difference between Chitosan and control sites (P>0.05). At 6 months, both sites showed defect fill with depth reduction over baseline measurements. Statistically significant difference between Chitosan and control sites when compared (P<0.05).

Table 2: The radiographic infra-bony defects depth of chitosan sites and control sites at various time intervals

	Chitosan sites				Control sites			
	At baseline*	At 6months**	Defect fill	Defect resolution (%)	At baseline	At 6 months	Defect fill	Defect resolution (%)
Range	3.5–7.5	1.5–4	1.5–3.5	36.5–62.5%	3.5–7.5	4.0–4.5	0.5–1.5	10.2-20.5%
Mean ± SD	5.1±0.5	2.2±0.6	2.8±0.4	56.75±12.5%	5.2±0.6	4.2±0.2	0.8±0.3	15.5±4.5%

Chitosan sites versus Control sites at: \*Baseline, not significant \*\*six months, P<0.05 significant



Fig.7: Preoperative periapical radiograph from periodontitis patient in the Chitosan sites, showing a 5 mm deep infra-bony defect on the distal surface of the first lower right molar



Fig.8: Six months postoperatively, showing evidence of 3 mm defect fill

Reference: Photographed by the author July 2015

#### 4. DISCUSSION

Chitosan has been reported according to many studies as effective biodegradable and biocompatible substance in repairing bone defects. Chitosan can be used as a biocompatible coating for orthopedic and dental implants with minimal inflammation reported. Moreover, Chitosan microparticles improved drug delivery that increase and accelerate bone growth. (Ezoddini-Ardakani, Navab Azam, Yassaei, Fatehi, & Rouhi, 2011; Kung et al., 2011; Y.-M. Lee et al., 2000)

Chitosan has been used in combination with different local dental biomaterials such as Glass ionomer cement (GIC) centrimide with chlorhexidine to intervene with bacterial-host interaction preventing the progression of caries, as well as dexpanthenol gel to enhance wound healing and certain oral anti-fungal mouth rinses, as chitosan contains itself potent anti-fungal properties. A specific chitosan brush would be necessary to deliver local applications of the formula. Bone repair and regeneration are possible due to the biocompatibility and non-digestive chitosan properties as mentioned earlier. (Mishra, Pandey, & Manickam, 2017; Pippi, Santoro, & Cafolla, 2017)

Based on a lot of studies investigated effects of chitosan on bone healing, various theories on its mechanisms was postulated. Such as, chitosan increases vascularization of blood vessels and stimulates budding tissue . (Chevrier, Hoemann, Sun, & Buschmann, 2007; Zhao et al., 2012)

Also, chitosan might be used on systemic deliveries with significant positive effects, especially on individuals where severe systemic diseases prominently affect oro-dental structures; such as neuromuscular disorders, cancer-associated osteosequestrectomy and osteoporosis where bone density is reduced and sustained-releasing fluoride effects are necessary to adapt adequate treatment modalities. Also, the ascorbic acid (Vitamin C) present on the human body helps activate chitosan in the intestines leading to less cholesterol and fat absorption , aiding patients on dialysis procedures; as well as increasing insulin levels and decreasing blood glucose, which directly promotes general health and diminishes major affecting issues occurring within the oral cavity. (Fookesa, Mengatto, Rigallib, & Luna, 2019)

Chitosan hydrogel formulation appears to be stable on neutral Ph levels and stable on an approximately 48 hour period, where sodium fluoride, calcium and phosphate's absorbability are most likely to be increased; on which it is crucial for bone defects repair . (Fookesa et al., 2019)

Babrawala, et al, (2016) in their 9 months clinical trial using 15% chitosan gel as a bone graft in treating intrabony defects reported a significant PPD reduction of  $5.8 \pm 1.39$  mm and a CAL gain of  $5.8 \pm 1.39$  mm. Moreover, a greater reduction in IBD depth of  $3.41 \pm 1.17$  mm and a defect resolution of  $80.49 \pm 7.50$  % at 9 months. And this comes in agreement to this study results.

On periodontology and implantology study fields, statistics were significant on clinical trials with moderate to minimal risk of bias, as chitosan brushing to remove dental biofilms were proved, stabilize bone layers, bleeding and healing sockets upon tooth extractions. (Ezoddini-Ardakani et al., 2011; Zeza, Wohlfahrt, & Piloni, 2017)

Chitosan can enhance platelet adhesion and aggregation.(Ezoddini-Ardakani et al., 2011) . High concentrations of platelets or platelet-rich plasma release high levels of PDGF and TGF- $\beta$ . (Jayasuriya & Kibbe, 2010) It was reported that chitosan can stimulate platelets to release these growth factors which are capable of regulating osseous- related activities. Platelets can contribute to mineralized tissue regeneration of by stimulation of the mitogenic activity of bone cells, It is likely that in Chitosan presence with platelets and related growth hormones enhance heterotopic bone formation involving differentiation of mesenchymal cells in connective tissue into bone-forming cells. (Jeong Park et al., 2000; J.-Y. Lee et al., 2002; Mizuno et al., 2003; Oktay et al., 2010; Zhao et al., 2012)

Compared with another study, (Boynueğri et al., 2009) in which Chitosan gel was applied for the treatment of chronic periodontitis and the reduction in PD values were reported as 1.21 mm for Chitosan, 1.48 mm for Chitosan metronidazole and 0.94 mm for control sites, our study showed slightly superior results confirming that the use of Chitosan in infrabony defects enhanced bone fills in periodontitis patients .However , future researches are needed to clarify the response to Chitosan treatment in different periodontitis stages and grades.

Similarly, Babrawala, et al, (2016) reported better results were in comparison with another study done by (Akncbay et al, (2007), where chitosan gel was applied for the treatment of chronic periodontitis. It was noted that after 6 months there was a reduction in PPD by 1.21 mm for chitosan and 0.94 mm for the control

Some infrabony defects in this study were three-walled defects, while others were combination of one and two walls. Cortellini et al. (Cortellini, Prato, & Tonetti, 1995) reported that two and three walled defects being highest potential for regeneration when grafting procedures were used. Moreover, there is strong evidence of better predictability with deep, narrow defects compared with shallow, wide ones. (Laurell, Gottlow, Zybutz, & Persson, 1998). However, it is challenging to control these variables in human clinical trials, since it is impossible to obtain matched osseous defects. Therefore, the potential influence of this variability on the results needs to be recognized.

When interpreting this study findings, it seems that gain in clinical attachment level concur with radiological findings. In addition, postsurgical healing revealed good soft tissue response to Chitosan gel with no complications. Furthermore, the patients' good standards of oral hygiene improved the treatment outcome.

Finally there is a need of well-designed studies to test novel regenerative approaches in the context of periodontal tissue regeneration with emphasis mainly on histologic evidence of periodontal regeneration.

## 5. CONCLUSION

Chitosan gel showed promising benefit in periodontal regeneration context among periodontitis patients. As it is a safe compound with no side effects observed, further researches should be carried to enroll chitosan on medical and dental practices. Moreover; modern new biomaterials should be improved to enhance their characteristics and increase the statistical significance clinically with very low bias for error and adequate criteria to carry any dental procedure involving periodontal tissues.

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