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The Use of Triphasic Hyaluronan-Chitosan-Strontium Chloride membrane in Treating Intrabony Defect "Randomized Clinical Trial"

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Abstract

Aim: The purpose of periodontal therapy is to halt the increasing deterioration by managing infection, hence preventing tooth loss. This study was to determine if a combination of strontium chloride membranes, hyaluronan, and chitosan would be beneficial in treating periodontal intrabony defect.

Methods: This randomized controlled trial included thirty six patients, ranging in age from twenty-five to fifty-five, participated in this study, they were split into two equal groups: Group B (Test group): patients received surgical treatment using hyaluronan, chitosan, and strontium chloride membrane; Group A (Control group) patients had open flap debridement.

Results: Group B experienced significantly less pain than group A at D1 and D2 ($P<0.001$), but the remaining durations were similar between the two groups. Groups A and B showed significant decreases in gingival index and probing depth at 3 and 6 months compared to baseline ($P<0.001$).

Conclusions: When addressing intrabony defects, the triphasic Hyaluronan-Chitosan-Strontium Chloride membrane was used in combination with periodontal flap surgery; nevertheless, there was no statistically significant change observed when compared to OFD alone. Both groups showed improvement in terms of radiographic bone fill, gingival index, clinical attachment loss, and periodontal probing depth. Furthermore, as evidenced by decreased discomfort and swelling, the tissue's reaction to the triphasic Hyaluronan-Chitosan-Strontium Chloride membrane was positive.

Keywords: Triphasic Hyaluronan, Chitosan, strontium Chloride membrane, Intrabony Defect.

Introduction:

In the field of dental health, periodontal diseases stand as a principal cause of tooth loss, presenting a significant challenge for both patients and dental practitioners. These conditions, characterized by an inflammatory response within the periodontium, can lead to the destruction of tooth-supporting structures, necessitating interventions that go beyond conventional treatment paradigms [1].

In order to stop this increasing deterioration and avoid tooth loss, periodontal therapy aims to manage infection. Nevertheless, even after nonsurgical periodontal therapy (NSPT), periodontal pockets related to intra-bony defects (IBD) frequently persist, raising the possibility of disease development and degrading the prognosis. As a result, surgery is frequently regarded as a viable alternative. According to available data, IBD patients receiving guided tissue regeneration (GTR) using biological membranes positioned to treat the affected area may experience tissue creation. This serves as a guide for the recovery procedure [2].

The cornerstone of treating this widespread illness has been traditional therapies for periodontitis, which include patient education, dental hygiene advice, scaling, root planing, and in certain cases, periodontal surgery or the use of chemotherapeutic medicines. Despite these efforts, the quest for enhanced recovery outcomes has led to the exploration of innovative materials and techniques in periodontal regeneration [3].

Using a triphasic hyaluronan-chitosan-strontium chloride membrane has become apparent as a viable therapeutic option for periodontal intrabony defect among these innovative techniques. Each component of this triphasic system brings unique properties that are beneficial to the regenerative process [4].

Chitosan, a biocompatible and biodegradable polysaccharide, is lauded for its antimicrobial properties and its ability to facilitate bone formation, owing to its structural resemblance to glycosaminoglycans. Because of this, it's a great scaffold material for tissue regeneration and medication administration. [5].

Hyaluronic acid, a key component of the extracellular matrix in connective tissues, plays a crucial role in wound healing. Its high molecular weight contributes to tissue hydration and facilitates cell migration, essential for the repair and regeneration of periodontal tissues. Its ability to modulate inflammation and promote angiogenesis further underscores its importance in creating a conducive environment for tissue repair [6].

Strontium Chloride, known for its osteogenic properties, enhances bone regeneration through the stimulation of periodontal ligament stem cells and the promotion of bone formation. Its inclusion in periodontal therapy can lead to significant improvements in clinical outcomes, such as reduced pocket depth and increased attachment levels, offering a new dimension to regenerative periodontal treatment [7].

Thus, the purpose of this study was to assess how well strontium chloride membranes, hyaluronan, and chitosan work together to repair periodontal intrabony defects.

Patients and Methods:

This study was a parallel-group, clinical, two-arm, actively controlled randomized controlled trial. It included thirty six patients were ranging in age from twenty-five to fifty-five. They were chosen from the Department of Oral Medicine and Periodontology's outpatient clinic at October 6 University's Faculty of Dentistry.

The study protocol and the template form for written informed consent were approved by the Research Ethics Committee, Faculty of Dentistry, 6 October University, after their assessment and acceptance by the Center of Evidence-Based Dentistry, 6 October University.

Inclusion criteria were patient having stage II to III periodontitis with probing pocket depths ≥ 5 mm and radiographic evidence showing infra bony defect, Grade B periodontitis, systemically healthy individuals, a probing depth of more than 5 mm after phase 1 therapy,

pocket depth is measured and if more than 5 mm, the surgery was done, compliant patients who follow oral hygiene instructions. While, Patients who had undergone periodontal or antibiotic therapy within the six months before the trial, smokers, women who were pregnant or breastfeeding, and those using drugs known to alter bone turnover were all excluded from the study.

The patients were split into the following two equal groups: Group B (Test group): patients received surgical treatment using hyaluronan, chitosan, and strontium chloride membrane; Group A (Control group) patients had open flap debridement.

Methods:

Membrane preparation

Membrane components were: Chitosan, Strontium Chloride, Hyaluronic acid powder, Glycolic Acid 70%, and Sodium hydroxide. Every chemical and reagent used was of analytical grade. Distilled water was utilized for the whole project.

The Chitosan, Hyaluronic acid, and Strontium Chloride membranes were prepared using freeze extraction [8]. The gelation method used by Ho et al. was implemented at the materials science department at Alexandria University's Institute of Graduate Studies and Researc [9].

Surgical procedures:

Presurgical protocol:

Prior to the procedure, all study-eligible patients underwent a thorough periodontal examination, and complete periodontal charts were acquired. For the purpose of diagnosing periodontitis patients, periapical radiographs were obtained at the areas of attachment loss. After the initial examination, all patients were motivated to perform personal oral hygiene measures using soft toothbrushes and interdental cleansing devices. Each patient underwent full mouth supra and sub-gingival debridement. All the previously listed clinical evaluations were examined to ascertain the suitability of the participants for the trials and the need for the surgery.

For every subject, the following measures were assessed: Plaque index (PI): With the exception of the third molars, the vestibular and lingual surfaces of every tooth are evaluated for the presence of dental plaque using the plaque index. After the teeth and gingiva had dried naturally, plaque was examined using a mouth mirror and an explorer. Using a range of criteria from 0 to 3, the four regions of the teeth that were systematically analyzed were the distofacial, facial, mesiofacial, and lingual surfaces. No plaque was indicated by a score of 0, individual plaque particles were indicated by a score of 1, a thin, continuous band of plaque (up to 1 mm) was indicated by a score of 2, and a band of plaque wider than 1 mm but covering less than one-third of the tooth's crown was indicated by a score of 4.

Bone sounding: measuring from the closest cusp tip of the involved tooth to the base of the defect (as a reference point) and the bone level of the defect using an incipient probe (15 mm).

Radiographic examination was performed just before the surgery using a size 2 imaging plate (Guilin wood pecker medical instrument COLTD) and dental x-ray machine which was set as 70 kvp,8 MA, and 0.08-0.04 s, the intra-oral radiograph was captured using a paralleling technique with kcp film hddc.

Surgical protocol

The envelope flap was started as an intrasulcular incision using the number 15 blade. The incision extended from the mid-buccal surface of the tooth mesial to the involved tooth to the mid-buccal surface of the tooth distal to the involved tooth. The flap was reflected buccally using a mucco periosteal elevator. If the required accessibility was not achieved then the palatal or lingual flap was reflected with the same extension as the buccal one. After flap elevation and root planing with a universal curette to remove soft and infected cementum as well as granulation tissue, the flap was reflected to expose 2 mm of bone apical to the defect base. A superficial-layer split-thickness flap was then performed, providing the maximum

amount of flap release and mobilization for coronal positioning. With the superficial-layer split-thickness flap technique, the muscle and periosteal layers beneath the flap remain attached to the bone, allowing for complete, passive flap coverage for almost all roots. The flap is dissected along the external surface contouring toward the lip or cheek, separating the epithelium and connective tissue from these layers. Then the membrane was applied in the area of the intrabony defect after contouring the external border using a surgical successor to be rounded and it was avoided to have any sharp edges as possible taking into consideration the dimension of the defect using a template, the application of the membrane was easy with no need for using any cementing material or more sutures for fixation.

Sutures were used to stabilize the coronal displacement of the buccal flap. The envelop incisions were closed with interrupted sutures [10-13].

Methods of Clinical Evaluation:

After surgery, patients were asked to come back one and two weeks later (for gingival index). At three and six months following therapy, the following clinical parameters were assessed for each patient included in the research [14, 15]: According to Löe and Silness (1963), gingival index (GI). Level of clinical attachment (CAL). Glavind and Löe (1967) defined periodontal probing depth (PD) and used an acrylic stent to measure pocket depth.

At the beginning of phase 1 treatment and then three and six months following surgery, radiographic measures were taken. Digital periapical X-ray was used to take radiographs. The following radiographic measures need to be mentioned: From the cemento-enamel junction to the base of the bony defect, the level of the bone height was measured. Bone sounding was also done three and six months following surgery.

Statistical analysis: SPSS v26 was used for statistical analysis. The two groups were compared using the unpaired Student's t-test, and readings were compared using the ANOVA (F) test. Quantitative data were provided as mean and standard deviation (SD). To investigate the frequency and percentage (%) of the qualitative variables, the Chi-square test was employed. A result was considered statistically significant if the two-tailed P value was less than 0.05.

Results:

Demographic data were insignificantly different between both groups. In both group A and group B, the clinical attachment loss was significantly lower after three months and after six months when compared to baseline (P <0.001). Nevertheless, neither group's clinical attachment loss at baseline, three months, or six months showed a statistically significant difference (**Table 1)**.

Table 1: Comparing demographics and clinical attachment loss at baseline, after 3 months, and after 6 months between the two groups

		Group A (n=18)	Group B (n=18)	P value	
Age (years)		33.5 ± 9.51	31.1 ± 7.93	0.430	
Gender	Male	9 (50%)	5 (27.78%)	0.171	
	Female	9 (50%)	13 (72.22%)		
		Baseline	After 3 months	After 6 months	P value	Post Hoc
Clinical attachment loss (Group A)		5.9 ± 0.35	0.3 ± 0.36	0.2 ± 0.32	<0.001*	P1<0.001* P2<0.001* P3=NS
Clinical attachmemt loss						
Clinical attachment loss (Group B)		6.2 ± 0.38	0.2 ± 0.38	0.2 ± 0.38	<0.001*	P1<0.001* P2<0.001* P3=NS
Group A (n=18)		5.9 ± 0.35	0.3 ± 0.36	0.2 ± 0.32	NS	
Group B (n=18)		6.2 ± 0.38	0.2 ± 0.38	0.2 ± 0.38	NS	

Data is expressed as the mean ±SD, P1: P-value comparing baseline reading and after 3 months reading, P2: P-value comparing baseline reading and after 6 months reading, P3: P-value comparing after 3 months reading and after 6 months reading.

In group A, pain was significantly reduced at all durations compared to D1 (P<0.001). Pain was significantly reduced at D3, D4, D5, D6, and D7 compared to D2 (P<0.001). Pain was insignificantly different among D3, D4, D5, D6, and D7. In group B, pain was significantly reduced at all durations compared to D1 (P<0.001). Pain was significantly reduced at D3, D4, D5, D6, and D7 compared to D2 (P<0.001). Pain was insignificantly different among D3, D4, D5, D6, and D7. The pain was significantly reduced in group B compared to group A at D1 and D2 (P<0.001), while the remaining durations were insignificantly different between both groups (**Table 2).**

Table 2: Pain in group A and B at different durations and Comparing pain at different durations between the two groups

		D1	D2	D3	D4	D5	D6	D7	P value
Pain (Group A)	Mean ± SD	7.6 ± 0.61	4.4 ± 0.62	1.1 ± 0.24	1 ± 0	1 ± 0	1 ± 0	1 ± 0	<0.001*
	Post hoc	P1	<0.001*	<0.001*	<0.001*	<0.001*	<0.001*	<0.001*	
		P2		<0.001*	<0.001*	<0.001*	<0.001*	<0.001*	
		P3			0.332	0.332	0.332	0.332	
		P4				NS	NS	NS	
		P5					NS	NS	
		P6						NS	
		D1	D2	D3	D4	D5	D6	D7	P value
Pain (Group B)	Mean ± SD	6.6 ± 0.62	3.3 ± 0.57	1.1 ± 0.24	1 ± 0	1 ± 0	1 ± 0	1 ± 0	<0.001*
	Post hoc	P1	<0.001*	<0.001*	<0.001*	<0.001*	<0.001*	<0.001*	
		P2		<0.001*	<0.001*	<0.001*	<0.001*	<0.001*	
		P3			0.331	0.331	0.331	0.331	
		P4				NS	NS	NS	
		P5					NS	NS	
		P6						NS	
Group A(n=18)	mean ± SD	7.6±0.61	4.4±0.62	1.1±0.24	1±0	1±0	1±0	1 ± 0	---
Group B(n=18)	mean ± SD	6.6±0.62	3.3±0.57	1.1±0.24	1±0	1±0	1±0	1 ± 0	---
P-value		<0.001*	<0.001*	0.968	NS	NS	NS	NS	---

P1: P-value comparing D1 reading and the remaining readings, P2: P-value comparing D2 reading and the remaining readings, P3: P-value comparing D3 reading and the remaining readings, P4: P-value comparing D4 reading and the remaining readings, P5: P-value comparing D5 reading and the remaining readings, P6: P-value comparing D6 reading and D7 reading. *: significant P value.

Between the two groups, the swelling score did not differ significantly during different time periods **(Table 3)**

Table 3: Swelling score in each studied group at different durations,

	D1	D2	D3	D4	D5	D6	D7	P value
Swelling Score (Group A)	1 ± 0	1 ± 0	1 ± 0	1 ± 0	1 ± 0	1 ± 0	1 ± 0	NS
Swelling Score (Group B)	1 ± 0	1 ± 0	1 ± 0	1 ± 0	1 ± 0	1 ± 0	1 ± 0	NS
Group A (n=18)	1 ± 0	1 ± 0	1 ± 0	1 ± 0	1 ± 0	1 ± 0	1 ± 0	----
Group B (n=18)	1 ± 0	1 ± 0	1 ± 0	1 ± 0	1 ± 0	1 ± 0	1 ± 0	----
P-value	NS	NS	NS	NS	NS	NS	NS	-----

In both group A and group B, the gingival index was significantly lower at three and six months compared to baseline (P<0.001), although it was not statistically different in any group at three or six months **(Table 4).**

Table 4: Gingival index in each of the studied groups at baseline, after 3 months, and after 6 months

	Baseline	After 3 months	After 6 months	P value	Post Hoc
Gingival index (Group A)	2.6 ± 0.15	0.7 ± 0.46	0.6 ± 0.5	<0.001*	P1<0.001* P2<0.001* P3=0.16
Gingival index (Group B)	2.1 ± 0.5	0.4 ± 0.51	0.3 ± 0.49	<0.001*	P1<0.001* P2<0.001* P3=0.16

Gingival index	Baseline	After 3 months	After 6 months
Group A (n=18)	2.6 ± 0.15	0.7 ± 0.46	0.6 ± 0.5
Group B (n=18)	2.4 ± 0.5	0.4 ± 0.51	0.3 ± 0.49
P-value	1	0.096	0.1

Data is expressed as the mean ±SD, P1: P-value comparing baseline reading and after 3 months reading, P2: P-value comparing baseline reading and after 6 months reading, P3: P-value comparing after 3 months reading and after 6 months reading.

The radiographic bone level was insignificantly different at baseline, after 3 months, and after 6 months in the two studied groups. **Table 5**

Table 5: Radiographic bone level in each of the studied groups at baseline, after 3 months, and after 6 months

	Baseline	After 3 months	After6 months	P value
Radiographic bone level (Group A)	5 ± 0.43	5 ± 0.12	4.9 ± 0.86	0.996
Radiographic bone level (Group B)	5.11 ± 0.75	5 ± 0.75	5 ± 0.74	0.996
Group A (n=18)	5 ± 0.43	5 ± 0.12	4.9 ± 0.68	---
Group B (n=18)	5.11 ± 0.75	5 ± 0.75	5 ± 0.74	----
P-value	NS	NS	NS	---

Data is expressed as the mean ±SD,

In both group A and group B, the probing depth was significantly lower after three months and after six months when compared to the baseline (P<0.001), although it was not statistically different in any group after three months and six months. Between the two groups, there was no significant difference in the probing depth at baseline, three months, or six months (**Table 6).**

Table 6: Assessing the difference in probing depth between the two groups at baseline, after three months, and after six months.

	Baseline	After 3 months	After 6 months	P value
Probing depth (Group A)	6.2 ± 0.38	0.2 ± 0.38	0.2 ± 0.38	<0.001* P1<0.001* P2<0.001* P3=NS
Probing depth (Group B)	6.2 ± 0.38	0.2 ± 0.38	0.2 ± 0.38	<0.001* P1<0.001* P2<0.001* P3=NS
Group A (n=18)	6.2 ± 0.38	0.3 ± 0.25	0.2 ± 0.25	----
Group B (n=18)	6.2 ± 0.38	0.3 ± 0.38	0.2 ± 0.38	----
P-value	NS	NS	NS	----

Discussion

Periodontitis stands as a principal cause of tooth loss. When an immune response is triggered by a degenerative inflammatory illness that affects the periodontium, the teeth's supporting components deteriorate[1].

The gingival index was observed to be significantly lower in group A and group B after three months and after six months compared to baseline (P<0.001), although it was not statistically different in either group after three months or after six months. At the beginning, three, and six-month marks, there was no significant difference in the gingival index between the two groups.

Mahmoud et al. separated 20 patients into two groups using the split-mouth approach in order to assess the clinical, radiological, and biochemical effects of 1% chitosan gel in the treatment of chronic periodontitis patients. Group A: 30 sides were given SRP along with 1% chitosan gel applied intrapocket. Group B: included thirty sides that were given SRP exclusively. According to the study's findings, there was a test group-specific statistically significant difference in gingival index between the study groups. The use of the gel form of Chitosan gel has sustained release property which may prolong the effect of the material, Hence, the difference in the gingival index between study groups [16].

The difference in the results between Mahmoud et al study and the current study may be due to two factors: a) the sample size in Mahmoud et al study was larger compared to the

current study, and the use of the gel form of Chitosan which has sustained release properties that could be responsible for more prolonged time for the material to act upon the tissue during the healing phase.

The findings of the present GI research are consistent with a trial comparing the clinical and radiographic effects of HA with SRP in the treatment of vertical bone loss in patients with periodontitis. In this investigation, the researchers found that the gingival index (GI) mean value for the HA group was 1.48 ±0.25 at baseline before to surgery, 0.633 ±0.12 three months later, and 0.60 ±0.10 six months later. Prior to surgery, the SRP group's baseline was 1.52±0.29. Three months later, it was 0.671 ±0.11, and six months after, it was 0.46 ±0.18 [17].

According to our findings, PPD decreased significantly in groups A and B after three months and six months when compared to baseline (P<0.001), although PPD did not vary statistically in either group after three months or six months. At baseline, three months later, and six months later, the two groups' PPDs did not differ significantly.

Consistent with this, chitosan was used in place of SRP in a research by Faghani et al. on the treatment of intrabony defects. Between the baseline and follow-up, they discovered that the mean PPD in the chitosan and SRP groups had dramatically decreased (P<0.05). Between the two groups, there was no significant difference in the pre-surgical PPD (P=0.316). Moreover, during follow-up, there was no significant change in PPD between the two groups (P=0.133) [18].

According to our findings, clinical attachment loss was not statistically different in groups A and B after three months or after six months when compared to baseline (P<0.001). However, after six months and after three months, clinical attachment loss was not significantly different in either group. Between the two groups, there was no significant change in the loss of clinical attachment at baseline, three months later, or six months later.

Additionally, Faghani et al. found that between baseline and follow-up, CAL improved in every group. Between the groups, there was no significant difference at baseline (P=0.402) or at follow-up (P=0.953). Nonetheless, there was a significant difference in CAL before and after surgery in every group (P<0.05) [18].

This study demonstrated that both groups (group 2 having open flap debridement with bone graft mixed with a chitosan nano hydrogel and group 1 having open flap debridement with bone graft as a control group) demonstrated significant decreases in probing pocket depths and CAL at six months. These findings were in contrast to those of Meenakshi and Sankari. In comparison to group 1, which had a mean decrease in probing depths of 8 ± 0.8 to 2.3 ± 0.7, group 2 (the test group) had a much larger mean reduction (8.3 ± 0.9 to 1.6 ± 0.8). Group 2 saw a significantly higher mean drop in CAL (8.7 ± 0.6 to 1.6 ± 0.8) compared to group 1 (8.6 ± 0.5 to 2.4 ± 0.7). This difference may be attributed to the added benefit of the use of bone grafts [19].

Using a chitosan membrane, the efficacy of a chitosan nano hydrogel as a periodontal regeneration material for the treatment of intrabony defects was examined. Twenty patients were randomly assigned to two groups: the test group got grafts combined with hydrogel of chitosan, while the control group got grafts made of bovine particles called osseografts, which were inserted into the defects. The results showed that the mean number of defect fills observed in groups 1 and 2 (3.5 ± 0.5 to 2.3 ± 0.4) from baseline to six months was recorded. At six months, there were statistically significant variations in the quantity of defect fill between the two groups. [19]. The combination of bone graft and Chitosan in the form of nanogel may have a beneficial effect over the use of Chitosan without a space provision material such as bone graft.

The strontium chloride membrane contains strontium (Sr), an alkaline earth metal that is a necessary trace element in human body. It may easily replace calcium in the bone matrix because to its intriguing characteristics and chemical similarity to calcium. It has been discovered that by promoting bone formation and decreasing bone resorption, it induces osteoblast activity. Furthermore, it has been shown in a number of studies to promote osteogenic differentiation and proliferation in osteoblasts and mesenchymal stem cells[20].

Kim et al. have recently concluded that chitosan helps promote bone formation because of its structural resemblance to glycosaminoglycans, which promotes osteoblast development and proliferation. Furthermore, chitosan has the ability to function as a vehicle for regulated medication release. The current study's findings indicated that chitosan significantly improved the identical group's clinical characteristics. These outcomes were in line with those of earlier studies that demonstrated significant improvements in CAL, bone level, and probing depth decrease at six months after using 1% chitosan gel. [21].

The hyaluronic acid component ensures optimal tissue hydration and inflammation modulation, chitosan provides a microbial-resistant scaffold that supports tissue and bone formation, and Strontium Chloride enhances bone regeneration and strength [22]

Conclusions:

The use of a triphasic Hyaluronan - Chitosan - Strontium Chloride membrane in combination with periodontal flap surgery to address intrabony defects did not demonstrate a statistically significant change when compared to OFD alone. Clinical attachment loss, periodontal probing depth, gingival index, and radiographic bone fill all showed improvement in both groups. Moreover, tissue response to the triphasic Hyaluronan -Chitosan- Strontium Chloride membrane was favorable as reflected by reduced pain and swelling.

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Conflict of Interest: Nil

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