EGYPTIAN
DENTAL JOURNAL
www.eda-egypt.org

Vol. 70, 221:233, January, 2024

Print ISSN 0070-9484 • Online ISSN 2090-2360

Oral Medicine, X-Ray, Oral Biology and Oral Pathology

Submit Date : 02-10-2023 • Accept Date : 08-11-2023 • Available online: 01-01-2024 • DOI : 10.21608/EDJ.2023.240207.2729

EFFICACY OF LOCALLY DELIVERED HYALURONIC ACID GEL AS AN ADJUNCTIVE TO NON-SURGICAL MANAGEMENT OF STAGE II OR STAGE III PERIODONTITIS: A RANDOMIZED CONTROLLED TRIAL WITH MICROBIOLOGICAL ANALYSIS

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ABSTRACT

Background: Non-surgical periodontal therapy, with or without adjunctive therapies, is an effective method in treatment of periodontitis. It decreases Pocket depth and results in formation of some new attachment**.** The comparison of local effects of non-surgical periodontal therapy only to scaling and root surface planning with the aid of 0.2% hyaluronic acid as local therapeutic agent regarding clinical parameters and microbiological analysis of main pathogenic periodontal pathogens (Aggregatibacter Actinomycetumomitans and Porphyromonus gingivalis) Using real time PCR was the aim of the study.

Subjects and methods: the current study was performed on twenty-eight patients diagnosed with localized periodontitis stage (II) or (III) grade (A). Patients were randomly divided into 2 groups with 14 participants in each. Group (I) "intervention group" candidates treated with scaling and root surface debridement with local application of 0.2% HA application in situ gel while group (II) had scaling and root surface debridement only. Microbiological indices were gathered at time interval: baseline, after 1 week and after 1 month.

Results: statistical results of our study showed advancement in MSBI, PD and CAL parameters in both groups after 1 and 3 months follow up. There was no statistically significant difference regarding microbiological analysis between 2 groups after 3 months.

Conclusion: we conducted from the current study that the application of 0.2% HA once in patients with stage II or III periodontitis had limited effect regarding clinical and microbiological analysis.

KEYWORDS: Periodontitis; Non-surgical therapy; Hyaluronic acid; Real time PCR.

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INTRODUCTION

Periodontal disorders are the most common dental problems. Gingivitis is an inflammation of the gingiva brought on by plaque and calculus accumulation. Periodontitis, an inflammatory condition of the tissues supporting the teeth caused by specific microorganisms or concentrations of specific microorganisms, causes the formation of periodontal pockets, gingival recession, or both, as well as the progressive destruction of the periodontal ligament and alveolar bone [1, 2].

Periodontitis is a multifactorial condition that is primarily brought on by particular bacterial strains that generate a number of harmful alterations that result in bone loss and loss of connective tissue connection. Numerous oral bacteria are thought to contribute to the etiology of periodontitis. Tannerella forsythesia (T.F.) and Porphyromonas gingivalis (P. G.) are thought to be the main causative organisms of this disease. Both are gramme-negative anaerobic rods. Also regarded as a major etiological organism for periodontitis is Trepenoma denticola (T.D), an oral spirochete [3-4].

A modified sorting of periodontal disorders was introduced by World Workshop in 2017 and now includes peri-implant disease, periodontitis, gingival problems, and periodontal symptoms of systemic diseases. When there is no clinical attachment loss (CAL), no bone loss, bleeding on probing (BOP), and a pocket depth of less than 3 mm, the periodontium is considered to be intact. Patients with stable periodontitis or those undergoing crown lengthening have better periodontal health due to the reduced periodontium they have [5].

The ability to define active periods of the disease and to better understand the disease process may both benefit from the confirmation of the microbial etiology of periodontitis. Knowledge for diagnosis and treatment can be easily obtained via microbiological analysis. In the meanwhile, tests are used for patients who have not reacted well to traditional therapy or to monitor patients who are in the maintenance phase in order to prevent the disease from recurrence [6].

The gingival sulcus can be utilized for collecting gingival crevicular fluid (GCF), which is a serum transudate or, more frequently, an inflammatory exudate. The fluid's components come from a number of different sources. GCF includes components from both the host and the microorganisms in the supra- and subgingival plaque. Blood molecules and deposits from periodontal tissues and cells are examples of host-derived constituents. The latter consists of the vasculature, epithelium, connective tissues, both mineralized and non-mineralized, as well as immune and inflammatory cells that have penetrated the periodontal tissues. Markers of inflammation, such as enzymes, cytokines, and interleukins, are among the significant host-derived components found in GCF. Furthermore, crevicular fluid can also contain the byproducts of tissue degradation [7].

Examples of qualitative approaches for periodontal assessment include enzymatic and PCR-based techniques. Enzymatic techniques are accessible, affordable, and don't need specialized equipment, but they are unable to distinguish between specific bacterial strains, making them unsuitable for deciding on antibiotics [8].

Although specific primers can be used in PCR techniques to identify specific strains of bacteria, this method has a significant drawback in that it cannot distinguish between dead and living bacteria because it uses chromosomal DNA as a template. Real-time PCR has therefore become an innovative technique for the detection of periodontal microorganisms. Its wide dynamic range of bacterial detection allows it to detect bacteria in any count and assess the association between these numbers and periodontal pocket depth, which is a significant advantage [9-10].

The most typical periodontitis treatment involves daily plaque control, as well as supra- and

subgingival calculus and plague removal. The goal of periodontal therapy is to replace lost periodontal tissue and provide an environment that is conducive to maintaining gingival health. However, in locations with restricted access, such as those with moderate to severe probing depths or furcation involvement, sufficient root instrumentation may not be possible. As a result, anti-microbial agent administration, either systemically or topically, has been employed as a supplement to traditional treatment. Studies have demonstrated that using adjunctive antimicrobial medications over treatments without them has additional benefits [11-16].

Systemic antibiotics have various restrictions since they must be administered at a certain dosage to produce the intended results. Additionally, systemic antibiotics result in negative side effects, drug resistance, inadequate tissue penetration, and failure to adequately concentrate at the infection site [17].

The therapeutic objective of local delivery drugs (LDDS) is accomplished by putting the antimicrobial agents entirely in the periodontal pocket, which makes the active drug in an immediate or controlled mode as an offensive against the infection while simultaneously minimizing its adverse effects [18].

Local drug delivery agents (LDDs) have a number of advantages over systemic antibiotics, including reduced dosage and frequency of drug administration, direct application at the site of infection, minimally invasive treatment, avoidance of GIT disruption, and accessibility to a variety of delivery methods. There are certain criteria for LDD agents, including biocompatibility, biodegradability, continuous release over an extended period of time, ease of administration, and inability to irritate the delivery site [19-20].

In the extracellular matrix of connective tissue, hyaluronic acid (HA), a glycosaminoglycan, can be discovered. It is made up of recurrent non-sulfated disaccharide units made of D-glucoronic acid and N-acetyl-D-glycosamine, which are connected by (1-3) and (1-4), respectively, glycoside linkages. HA serves a variety of purposes, including ion exchange filtering, promoting cell migration, playing a large role in space maintenance, providing a medium for hydration, tissue repair, promoting wound healing, angiogenesis, acting as an anti-inflammatory, and inducing heat shock proteins [21].

Due to these various qualities, HA has been used in the field of medicine for a variety of purposes, including tissue engineering, pharmacology, ophthalmology, orthopaedic surgery, plastic surgery, and gynaecology [22].

It has been thought that HA could assist with managing periodontitis due to a variety of its features. HA is the most prevalent higher molecular weight glycosaminoglycan in the extracellular matrix of periodontal tissue. The molecule HA is an enormous, highly negatively charged hygroscopic molecule. Huge amounts of water may be absorbed and retained owing to this feature, which puts pressure on the tissue around it and causes it to expand. This property also assists with shock absorption, space filling, and protein exclusion. This hygroscopic property results from a hydrogen bond formed when the N-acetyl group and neighboring carboxyl group are combined in an aqueous solution. Additionally, it has an anti-inflammatory and bacteriostatic action [23- 24].

The viscoelastic nature of HA facilitates periodontal procedures by maintaining space and protecting the surface. This nature can hinder the spread of viruses and bacteria, which is a crucial factor in periodontal therapy. Furthermore, the biocompatibility and non-immunogenic properties of HA have led to its widespread use in medical practice. Hyaluronan is cross-linked and esterified to provide the gel some rigidity and structure for the purposes of cell seeding [23-24].

The drug showed sustained release *in vitro* and released 80% in 14 days.[25].It has a distinctive

features such as scavenger-like ability to remove prostaglandins, metaloprotinases, and other bioactive molecules, HA has an anti-inflammatory effect [26]. Additionally, HA has an antioxidative impact by scavenging reactive oxygen species and is antiedematous due to its osmotic action, which aids in stabilizing the granulation tissue matrix [26-27].

Inflammation, granulation tissue creation, epithelium formation, tissue maturation, and tissue remodeling are the several stages of periodontal wound healing. Chemoattraction of cells initiates the sequence of actions. Each phase of the healing process for periodontal wounds involves hyaluronan [28].

By interacting with the fibrin clot, hyaluronan helps provide a structural framework during the inflammatory phase. In addition to phagocytosis of microorganisms, it plays a significant role in the migration and adhesion of macrophages and PMNs to the site of injury. These functions make it easier to inhibit the colonization and growth of anaerobic pathogenic bacteria [29].

However, the use of real time PCR to analyze quantitative changes of pathogenic periodontal bacteria has not yet been elucidated. We hypothesized that hyaluronic acid may has a major role to be used as an adjunctive to non-surgical treatment in periodontitis patients clinically and microbiologically.

SUBJECTS AND METHODS

Subjects

Periodontitis patients were chosen from the faculty of dentistry at Ain Shams University's oral medicine and periodontology department's outpatient clinic. The Research Ethics Committee gave its approval to this study. (ID: FDASU-Rec IM 16). and registered at (https://clinicaltrials.gov/ ID; NCT05834517)

Sample size calculation:

The study included a total of twenty-eight (28) patients with stage II or stage III periodontitis. A power analysis was created to have enough power to apply a 2-sided statistical test to the research hypothesis (null hypothesis), which is that there is no difference between the tested groups. Based on the findings of [30], an effect size (1.14) was estimated using an alpha () level of 0.05 (5%), a beta () level of 0.20 (20%), and a power of 80%; The number of instances in the projected sample size (n) was (26) with 13 in each category. In order to make up for the loss in follow-up, the sample size was raised to 28 (14 in each group). The sample size calculation was carried out with G*Power 3.1.9.4 [31].

Primary outcome measures

Plaque index (PI), Sulcus bleeding index (BI), Probing pocket depth and clinical attachment level (CAL) were the primary outcome measures.: The periodontal conditions of each patient were evaluated at baseline, after 1month and after 3 months follow-up. Plaque Index (PI) was used to assess the plaque accumulation around the gingival margin. Mean Sulcus Bleeding Index (MSBI) was used to assess gingival inflammation. Probing Depth (PD) and Clinical Attachment Level (CAL) were measured by UNC-15 probe. The occlusal stent was used as an auxiliary tool for the proper placement of the probe.

Secondary outcome measures

Quantitative changes of pathogenic periodontal bacteria (Porphyromonus gingivalis and Aggregatibacter Actinomycetumomitans) in the GCF as a secondary objective.

Study design and patient grouping:

This study was designed to be a Randomized, controlled, single blinded, parallel design, two arms clinical trial. The eligible participants were randomly allocated for one of the two groups; test and

control group using computer generated random tables (www.randomizer.org). The out-comer assessor was blinded to the type of the intervention and the whole study was carried out from May 2022 to December 2022.

Sample grouping

Twenty-eight (n = 28) Patients who were diagnosed as having stage II or stage III periodontitis were invited to enroll in the study. They had no systemic complicating factors which might have a negative impact on the healing response. In addition, they were not allergic to HA such as erythematous edema [32]. They must have pocket depth ≥ 5mm with horizontal bone loss, and less than 30% of teeth were affected. Subjects were excluded from the study if they were smokers, pregnant or lactated, took an antibiotic within the previous 6 months and received periodontitis treatment within the previous 6 months. Subjects who met the above criteria were explained about the study and those who decided to enroll in the study had to sign the informed consent. Patients are then divided randomly into 2 groups; **Group I:** test group (n = 14) patients were subjected to full mouth debridement followed by local delivery of 0.2% hyaluronic acid as an adjunctive treatment. **Group II: Control group** (n=14) patients were subjected to full mouth debridement only.

Treatment protocol and intervention

At day 1, after baseline parameters were recorded, full mouth scaling, root planing using hand instruments and ultrasonic scalers under local anesthesia -if needed- for patient's comfort were performed.

For group 1 patients one day after phase 1 therapy: After selection of the deepest

periodontal pocket which is equal to or more than 5mm site. The area around the site of the delivered materials was isolated by cotton rolls. The Hyaluronic acid (0.2% hyaluronan gel "gengigel R" marketed by Ricerfarma pharmaceuticals, Milan, Italy) loaded by the operator in a syringe with blunted tip then it was applied gently and removed slowly in order not to harm the tissue. The pockets were filled until the materials were detected at the gingival margin [33]. The participants had single application of 0.2% hyaluronic acid [34,35]

Subjects were informed not to drink, eat or rinse within 1 h after gel application and were not allowed to use any chemotherapeutic mouth rinse and oral irrigator throughout the study period. All participants were followed up for 12 weeks.

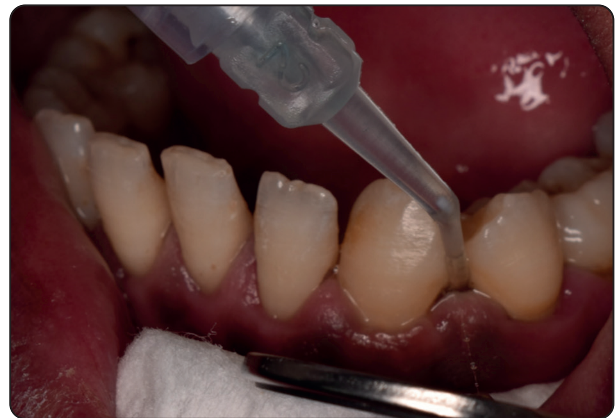

Fig. (1) Showing local application of gengigel using syringe with blunted tip gently.

Microbial Assessment

Gingival crevicular fluid was obtained from each patient. Only one site per subject was selected as a sampling site in periodontitis patients showing the deepest PD and CAL with signs of inflammation after phase 1 therapy (i.e. bleeding on probing) along with radiographic evidence of alveolar bone loss would be selected for the sampling and the same test site was selected for sampling after periodontal treatment [36].

The ideal in bacterial infection is to take a baseline sample, then after one week, the 3rd sample after two weeks or one month according to the time needed for healing thatis why GCF samples

were taken for bacterial load assessment at baseline, after 7 days from the last full mouth debridement, and 30 days after therapy [37-38]. The GCF fluid was collected by inserting perio-paper (Oraflow Inc., Smithtown, NY, USA) until resistance was felt into the pocket for 30s. Perio-paper strips visually contaminated with blood were discarded. Samples were immediately placed into a sterile, labeled Eppendorf tube and stored at -20ºC for subsequent assays [39]. The estimation of quantity of pathogenic periodontal bacteria in the analyzed samples was done using multiplex PCR technique.

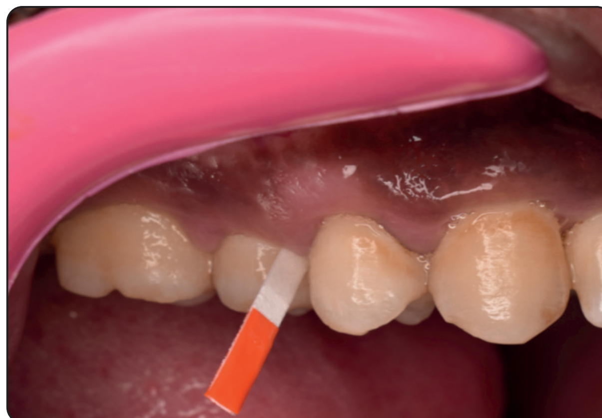

Fig. (2): GCF sampling using perio-paper strips just 0.5 mm into the sulcus and kept for 30 seconds [34].

Clinical assessment:

The periodontal conditions of each patient were evaluated at baseline, after 1month and after 3 months follow-up. Plaque Index (PI) was used to assess the plaque accumulation around the gingival margin. Mean Sulcus Bleeding Index (MSBI) was used to assess gingival inflammation. Probing Depth (PD) and Clinical Attachment Level (CAL) were measured by UNC-15 probe. The occlusal stent was used as an auxiliary tool for the proper placement of the probe.

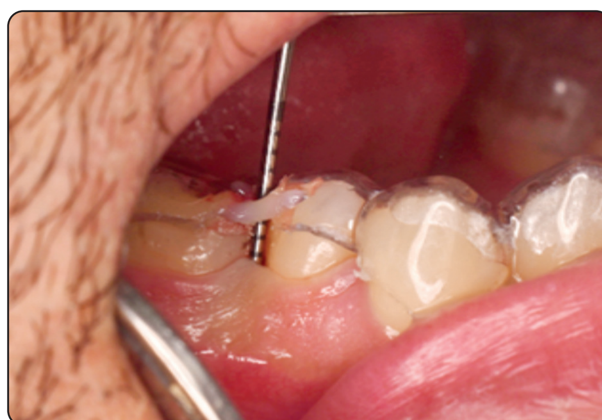

Fig. (3): preoperative Measuring of periodontal pocket depth using UNC-15 probe .

Statistical analysis

The Statistical Package for Social Sciences (SPSS) version 20 was used for data management and statistical analysis. The mean, standard deviation, median, and range were used to summarize numerical data. By examining the data distribution and performing the Kolmogorov-Smirnov and Shapiro-Wilk tests, data were examined for normality.

Independent t tests were used to compare groups with regard to normally distributed numerical variables. The paired t test was used to compare the baseline and 3-month observations.

Using the Mann Whitney U test, comparisons between groups were made with regard to non-parametric numerical variables, values of difference,

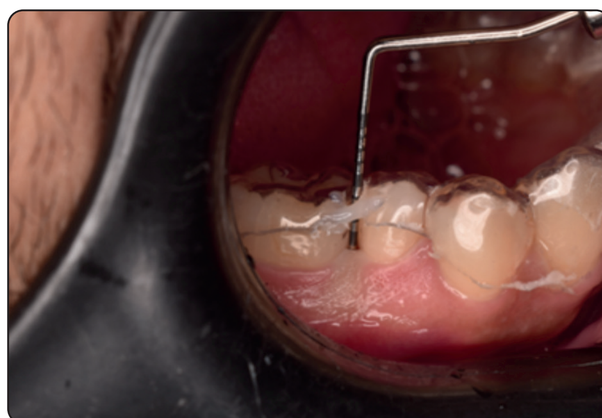

Fig. (3): postopertive Measuring of periodontal pocket depth using UNC-15 probe.

and percent change. Wilcoxon signed rank test and Friedman test were used to compare various observations.

The formula used to get the percent change was (value after-value before) / (value before-value before) X 100.

P-values are always two-sided. P-values 0.05 or lower were regarded as significant.

RESULTS

Twenty eight out of twenty-eight subjects completed the study. The mean age in group I (SRP and gel application) was (34.36±5.87), in comparison to (34.35±6.32) in group II (SRP only). The difference between groups was not statistically significant (p=1).

Gender: Group I (SRP and gel application) consisted of 7 males (50%) and 7 females (50%). Group II (SRP only) consisted of 7 males (50%) and 7 females (50%), with no difference between groups (p=1). None of the subjects complained or experienced adverse reactions after gel application.

Clinical parameters

At baseline, plaque index, sulcus bleeding index, PD and CAL were not significantly different between groups. After 3 months, plaque index, sulcus bleeding index, PD and CAL were significantly different when compared with baseline in both groups. However, comparison between groups revealed a similar change in plaque index, sulcus bleeding index, PD and CAL over time. Thus, there was no significant difference in plaque index, sulcus bleeding index, PD and CAL between groups at any time point.

Regarding the microbiological analysis of the Porphyromonus gingivalis and Aggregatibacter Actinomycetumomitans present within the GCF, after treatment there was a statistically significant decrease in the microbiological load in both groups after one week and one month postoperatively. However, comparison between real time PCR results of Bacterial DNA of Aggregatibacter Actinomycetumomitans and Porphyromonus gingivalis between the study and control group revealed no statistically significant difference between the 2 groups at baseline and after treatment.

TABLE (1) Descriptive statistics and test of significance difference between Probing depth (PD), Clinical attachment level (CAL), Sulcus Bleeding Index (BI) and plaque index (PI)

Group comparison (Mean ± SD)	Baseline	After 3 months	Between group comparison Comparison of slopes	Within group comparison
PD				
Intervention group	5.21±0.43	3.64±0.50	**0.299** ^{ns}	**<0.001***
Test group	5.07±0.27	3.43±0.51	**0.272** ^{ns}	**<0.001***
CAL				
Intervention group	5.71±0.83	3.93±0.92	**0.881** ^{ns}	**<0.001***
Test group	5.79±0.89	3.86±0.95	**0.941** ^{ns}	**<0.001***
BI				
Intervention group	1.50±0.94	0.36±0.63	0.745^{ns}	0.002
Test group	1.43±0.65	0.21 ±0.43	0.605^{ns}	0.001
PI				
Intervention group	1.64±0.84	0.93 ±0.62	0.386 ^{ns}	0.005*
Test group	1.93±0.73	1.21±0.70	0.256 ^{ns}	0.002*

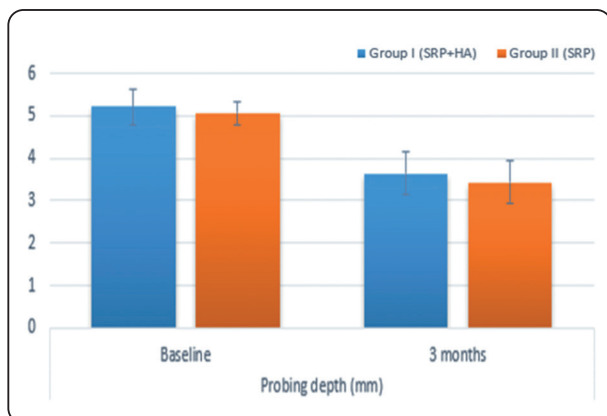

Fig. (4): Bar chart showing mean and standard deviation values of PD (mm) for different groups.

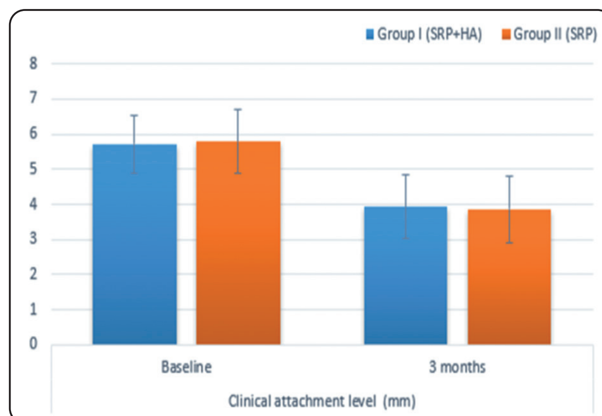

Fig. (5): Bar chart showing mean and standard deviation values of CAL (mm) for different groups.

TABLE (2) Descriptive statistics of bacterial DNA Aggregatibacter Actinomycetumomitans (AAC) and Porphyromannos Gingivalis (PG) (Bacterial copies/µl), intragroup (Friedman test) and intergroup comparisons (Mann Whitney U test)

(Mean ± SD)	Baseline	After 1 month	Between group comparison Comparison of slopes	Percentage change (%)
Aggregatibacter Actinomycetumomitans				
Intervention group	3.26±2.65	0.83±0.85	**0.748 ns**	-43.27±58.96
Control group	2.50±2.57	0.79±0.62	**0.748 ns**	-22.21±126.68
Porphyromonus gingivalis				
Intervention group	1.41±1.63	0.95±56	**0.319 ns**	48.14±170.17
Control group	2.20±1.53	1.07±0.51	**0.004**	28.57±268.17

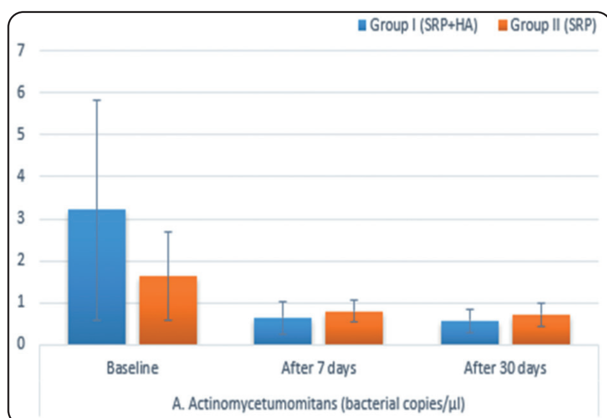

Fig. (6): Bar chart showing mean and standard deviation values of A. actinomycetemcomitans for different groups.

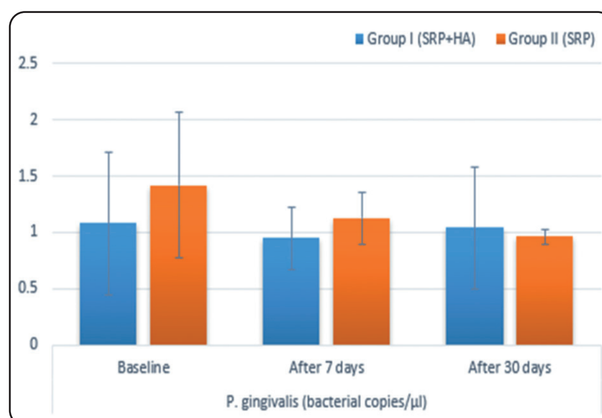

Fig. (7): Bar chart showing mean and standard deviation values of P. gingivalis for different groups.

DISCUSSION

Periodontal therapy's main goal is to prevent fragmentation and restore the periodontal apparatus to its normal form and composition. Periodontitis patients have been recommended to start with non-surgical periodontal therapy (NSPT), which includes scaling and root surface debridement (SRD). Even though a large amount of research has demonstrated that this mechanical debridement is helpful in reducing inflammation and the clinical manifestations of the disease, phase I therapy alone cannot bring the disease into remission or full tissue healing. Therefore, systemic or local adjunctive therapies should be used to assist SRD patients [40- 41].

Gram-negative anaerobic rods are linked to a mixed infection that causes periodontitis. (P.G., T.F., and T.D.). Therefore, figuring out whether these organisms are present is crucial for determining the severity of periodontal disease. The "red complex" [42] was the name given to these organisms. Qualitative identification is ineffective for diagnosing periodontitis because periodontal bacteria can be identified in both infected and uninfected pockets. The result was the development of real-time polymerase chain reaction (PCR) technology for quantitative detection [43].

LDDs are more effective at treating periodontitis than systemic antibiotics because they exist in the periodontal pockets directly. LDDs provide a number of benefits over systemic drugs, such as minimum invasiveness, dose reduction, avoidance of digestive issues, and better drug dispersion in the afflicted location, which results in the total eradication of periodontal bacteria. The benefit of this technique of treatment is that the drug remains in the pocket for up to several weeks with a concentration higher than the minimum inhibitory concentration (MIC). Consequently, a variety of LDD systems using various antibiotics or antiseptics have been created [44].

Qualitative detection is not appropriate for the diagnosis of periodontitis because periodontal pathogens can be found in both healthy and diseased sulcus. A quantitative detection system that uses real-time polymerase chain reaction (PCR) technology was created for this purpose [45].

HA has no immunogenic properties and is biocompatible. Esterification and cross-linking, two changes to HA that give it a gel-like structure and stiffness for cell-seeding efficiency. Additionally, HA eliminates MMPs, prostaglandins, and other bioactive compounds by acting as a scavenger. Additionally, it scavenges by limiting reactive oxygen species, which helps to stabilize the granulation tissue [26-28].

The anti-edematous property of HA is combined with an osmotic action. By altering the environment of the surrounding cells and promoting extracellular matrix infiltration, HA can enhance cellular behavior. Additionally, HA is thought to speed up the healing of tissue wounds by enhancing a number of cellular processes like identification, motility, and proliferation that make HA more receptive to colonization by cells that promote tissue repair. Additionally, when its molecular weight is low, HA is angiogenic, and when it is high, it is antiangiogenic. molecular weight high HA enhances osteoinduction when treating wounds [28].

Plaque index score was noted to have decreased statistically significantly in both the test group and the control group, and there was no statistically significant difference between the two groups at baseline or three months postoperatively. Additionally, the test group's mean percentage change is greater than the control groups. As a result, it was noted that the patients were complying and followed the recommended oral hygiene guidelines with regard to this criterion.

Despite the mean percentage change of the modified sulcus bleeding index showed no statistical substantial difference between these groups after 3 months follow up, there was a statistically significant decrease in each of the two studied groups from baseline to after 3 months and that was due to the

resolution of the inflammation and reduction of pro-inflammatory markers.

In two groups of our study the mean clinical attachment loss was decreased after 3 months postoperatively. Thus, attachment was regained but there was no significant difference in the mean percentage change between the test and control groups at time intervals.

With reference to periodontal pocket depth (PD), the results of the present study showed significant decrease in pocket depth in both groups from baseline to three months. However, by comparing the study group with the control group, there was no statistically significant difference between them after 3months.

Comparing Results of real time PCR results of Bacterial DNA of Aggregatibacter Actinomycetu-momitans bacteria between the study and control group regarding the mean change of microbial value in the interval (baseline-1month) revealed no statistically significant difference between the 2 groups.

Comparing Results of real time PCR results of Bacterial DNA of P.gingivalis bacteria between the study and control group regarding the mean change of microbial value in the interval (baseline-1month) revealed no statistically significant difference between the 2 groups.

The study made by ***Xu et al.*** *[45]* in 2004 used conventional PCR technique for microbiological analysis which not provide accurate data as periodontal pathogens would be available in periodontal pocket before and after periodontal treatment that necessitate the need to use qPCR to assess the amount of these periodontal pathogens.

The results of study conducted by ***Johassen et al. [47]*** in 2009 showed that the test group who receive 0.8% after SRP showed great reduction in BOP and PD when it compared to test group, this may be attributed to different concentration of HA.

The results of the study are similarly coinciding with study conducted by ***Gontiya and Galgi*** **[48]** ***in 2012*** that illustrated that application of 0.2% HA gel a long with SRP provide no additional benefit regarding periodontal parameters.

A study by ***Eick et al.*** **[49]** in 2013 conducted that the adjunctive application of HA had a positive effect in PD reduction and reduce the colonization of periodontal pathogens. In this study all participants used mouth wash twice daily with the application of 0.2% HA also twice daily by the patients. Moreover, they use 0.8% HA immediately after SRP. Also, microbiological analysis was done using conventional PCR which has certain limitations.

In addition, results made by ***Sahayata et al. [50]*** in 2014 using anaerobic bacterial culture didn't show any statistically significant outcome. This may be attributed as they used qualitative methods for periodontal diagnosis. To add more, this study was made to assess the effect of HA in patients with gingivitis.

The result of the study done by ***Olszewska-Czyz et al.*** **[51]** ***in 2021*** are similarly coinciding with the result of the study that concluded that topical application of 0.2% HA as an adjunctive to SRP didn't show any clinical significance when comparing the test group with the control group.

Mahmoud et al. **[52]** in 2022 concluded that the application of 0.2% HA gel and metronidazole when it applied locally as an adjunctive to non-surgical therapy had a useful effect on clinical periodontal treatment. This study had some limitations due to short follow up period (7 days only), they didn't use biochemical or microbiological analysis and they didn't have control group.

CONCLUSION

We conducted from the current study that the application of 0.2% HA once in patients with stage II or III periodontitis had limited effect regarding clinical and microbiological analysis. In addition, we also recommended more studies and investigations to evaluate multiple applications and different concentrations of HA in situ gel in the management of periodontitis.

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