Does Adjunctive Use of Hyaluronic Acid Improve Clinical Outcome of Mechanical Therapy for Cases of Mild Aggressive Periodontitis?

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Hyaluronic acid is an essential component of the periodontal ligament matrix and it has shown a number of clinical therapeutic properties, especially an anti-inflammatory effect on the gingival tissue. The aim of this study is to evaluate the potential benefits of using hyaluronic acid gel in topical application as an adjunct to mechanical therapy in the management of aggressive periodontitis. Results show an obvious improvement of clinical parameters, especially regarding the evolution of healing of the gingival tissue after periodontal therapy. Nevertheless, the antimicrobial effect needs to be proven in further studies.

Keywords: hyaluronic acid, aggressive periodontitis, periodontal pathogens, gingival inflammation

Aggressive periodontitis is a complex infectious periodontal disease that is characterized by a rapid and severe destruction of the periodontium leading to early tooth loss if left untreated [1]. It is associated with the presence of certain microbial species, such as Aggregatibacter actynomicetemcomitans, Porphyromonas gingivalis, Treponema denticola and Tanerella forsythia [2].

Current protocols suggest that early recognition of aggressive periodontitis and mechanical therapy combined with the use of antibiotic therapy, as a first phase of periodontal treatment, may lead to significant clinical improvements in the disease evolution [3]. However, the growing development of resistance to antibiotics, shown by multiple periodontal pathogens, as well as drug interactions, may be a considerable reason to limit the use of systemic antibiotics, especially if this particular form of periodontal disease has just set on [4]. Locally applied therapy has the advantage of a high concentration of the antimicrobial avoiding a considerable number of side effects [5,6] .

Hyaluronic acid (HA) is an extracellular component of the connective tissue. Studies have shown that it plays an important role in post-inflammatory tissue-regeneration and it has a number of clinical therapeutic properties. HA as a bactericidal agent is still controversial [7]. Hyaluronan gel is effective in controlling inflammation and gingival bleeding. Studies have documented reduction in the depth of gingival pockets along with a significant reduction in epithelial and lymphocyte cell proliferation with the use of HA gel [8]. 0.2% Hyaluronan containing gel has a beneficial effect in the treatment of plaque induced gingivitis [9]. The topical application of an HA-containing preparation represents a potentially useful adjunct in the therapy of gingivitis, although its use does not diminish the need for plaque reduction as a primary therapeutic measure [10].

The purpose of this study was to evaluate the clinical effects of a 0.2 % HA gel used as an adjunct in multiple applications after SRP in patients diagnosed with mild aggressive periodontitis.

Experimental part

A written signed consent for each patient and the approval of the Ethics Commission were obtained, after informing the subjects about the nature of the study.

The study was designed as a split-mouth study, on twenty three young patients diagnosed with mild generalized aggressive periodontitis. The mean age of the subjects was 31.17, 14 females and 9 males were selected based on the clinical diagnosis. Patients with previous periodontal treatment or use of antibiotics in the last 6 months as well as systemic health problems or pregnancy were excluded. Inclusion criteria was the presence of at least 20 natural teeth and at least two sites in each quadrant with a minimum probing depth of 5 mm. Four sites for each patient, with a minimum probing depth of 5 mm, were chosen as control and test sites, in different quadrants, in the molar and premolar area. Incisors and canines were excluded to avoid carry-over effects between test and control sites.

The following clinical parameters were recorded at baseline, 8 and 12 weeks after mechanical therapy for the selected sites: bleeding on probing (BOP), recession (REC), suppuration (SUP), plaque score (PS), probing depth (PD) and clinical attachment level (CAL). The measurements were performed by a single examiner with a conventional periodontal probe. BOP, SUP and PS for the two test and control sites, were assessed as present or absent. A score of 0 for absent and 1 for present was assigned to each site. PD and REC were measured in mm with a conventional periodontal probe, while CAL was calculated in mm, based on the previous measurements.

Subgingival plaque samples were taken with sterile paper points from the selected test and control sites prior to clinical examination, at baseline and at 8 and 12 weeks. Four pathogens, Aggregatibacter actynomicetemcomitans (Aa), Porphyromonas gingivalis (Pg), Treponema denticola (Td) and Tanerellla forsythia (Tf) were determined in each plaque sample by polymerase chain reaction (PCR). The PCR results were expressed as total counts of selected periodontal pathogens.

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Full mouth scaling and root planing (SRP) with hand instruments was performed for each patient. Two periodontal pockets with minimum probing depth of 5 mm in the molar and premolar area were selected in the first and third quadrant as control sites, where only SRP was performed. Other two sites in the second and forth quadrant, also in the molar and premolar area, were chosen for the subgingival application of a 0.2% HA preparate after SRP. The topical HA gel was applied immediately after SRP, and then, once a day, every day for the next week, by a clinician. The following 7 weeks, it was administered in the selected sites only once a week, by the same clinician.

Statistical analysis was performed using SPSS version 2.0 software program. Demographic parameters such as age were calculated as mean± standard deviation (SD). BOP, PS, SUP assessed as present or absent were expressed as percentages while PD, REC and CAL were calculated as mean ± SD (mm). The level for each periodontal pathogen tested was registered and a mean count ± SD was computed for the three determinations, for both control and test sites. Non-parametric tests (Kruskal-Wallis for 3 samples one way-ANOVA)was used to achieve the statistical significant difference in clinical and microbiologic parameters between baseline, 8 weeks and 12 weeks examination for both test and control sites, intra- and intergroup. $p<0.05$ was chosen as statistically significant.

Table 1
THE RESULTS FOR CLINICAL PARAMETERS AND PERIODONTAL PATHOGENS FOR THE STUDY GROUPS

	Control sites			Test sites			
Clinical Data	**Baseline**	**8 weeks**	**12 weeks**	**Baseline**	**8 weeks**	**12 weeks**	**P value**
PD (mm; mean ±SD)	5.70±.0635	3.83±0.57	4.09±0.66	5.78±0.67	3.61±0.58	4.00± 0.67	0.699
REC (mm; mean ±SD)	0.61±0.83	1.65±0.64	1.39±0.83	0.48±0.59	0.37±0.72	0.34±0.81	**0.000**
CAL (mm; mean ±SD)	3.26±1.42	2.04±0.63	2.09±0.73	3.17±1.55	2.00±1.34	2.13±1.32	0.957
PS (%)	73.91	43.47	34.78	78.26	26.08	30.43	**0.024**
BOP (%)	86.95	26.08	30.43	95.65	13.04	8.69	**0.002**
SUP (%)	39.13	8.69	13.04	30.43	4.34	4.34	**0.000**
Pathogens mean±SD							
Aa	186900.00±386275.388	24495.65±49963.764	27695.65±51403.426	149508.70±361493.514	48804.35±125240.382	74304.35±195221.421	0.564
Pg	289008.70±717619.627	22193.91±25286.071	19937.39±24425.679	271366.09±557596.641	58464.78±187657.257	64517.83±196534.914	0.489
Td	92045.22±158078.059	6280.87±14082.645	2900.87±9965.065	18056.52±1249858.212	12102.61±18181.718	7016.52±11993.398	0.676
Tf	123361.30±196234.890	415.22±1027.149	204.35±712.415	83578.70±161943.401	344.78±751.676	388.70±892.404	0.992

Results and discussions

Clinical data and microbiologic results measured for control and test sites, as well as the statistical significance ($p<0.05$), are shown in table 1.PD (mm) measured in control sites (mean± SD) at baseline was 5.70±.0635 (mm), at 8 weeks it has shown a slight decrease (3.83±0.57 mm), while after 12 weeks it has the tendency to increase (4.09±0.66 mm). PD for the test sites had the following values: 5.78±0.67 (mm) baseline, 3.61±0.58 (mm) at 8 weeks and 4.00± 0.67 (mm) at 12 weeks recall. There is no statistical difference between control sites and test sites concerning this clinical parameter ($p=0.699$). Furthermore, no significant statistical difference ($p=0.957$) was registered regarding CAL between the two sites, although it has almost stable values after SRP with or without HA. For the control sites, PS decreases after 8 weeks (43.47 %), continuing to decrease after 12 weeks (34.78%). However, for the test sites, even though it decreases majorly after 8 weeks (from a value of 78.26% to 26.08%) it shows a tendency to increase after 12 weeks (30.43%). A statistical significant difference ($p=0.024$) was computed for PS between groups. Plaque reduction does not necessarily occur as an effect of periodontal therapy. It mostly depends on the patient‘s compliance and understanding of importance of an adequate plaque control. The most significant differences registered between control and test sites were registered for BOP, REC and SUP. A major reduction for BOP in test sites(baseline value 95.65 %) was found after 8 weeks (13.04 %) and after 12 weeks (8.69%) while for the control sites, although initially it decreases (26.08%) , at the 12 weeks recall, it shows a slight tendency to increase (30.43%). REC shows the most spectacular evolution in values, for the test sites, decreasing throughout each recall session, while in the control sites it increases. A statistical significance ($p=0.000$) was established. SUP remains stable between 8 weeks and 12 weeks for the sites where 0.2% HA gel was applied, while for the control sites, it shows the same tendency as BOP, namely to increase.

Microbiologic results have registered a decrease for all tested periodontal pathogens after SRP with or without using HA as an adjunct. There were no statistical differences between groups for both 8 weeks and 12 weeks recalls (table 1). The microbial changes following initial periodontal therapy are depicted in figure 1.

In this study, SRP with and without adjunct use of 0.2% HA gel has shown, in the 8 weeks recall, in an improvement in all clinical and microbiologic parameters. A main difference in clinical parameters‘ evolution, between the two groups, can be noticed only after 12 weeks. The results

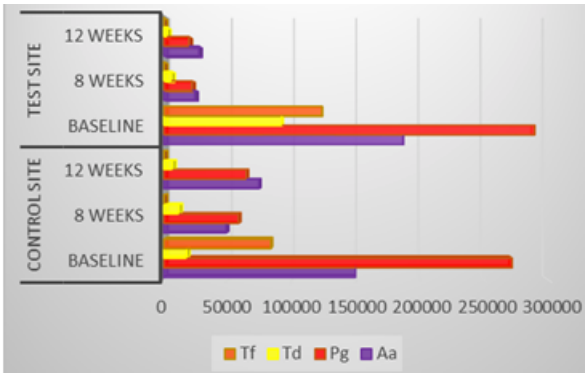

Fig. 1. Periodontal Pathogens' Evolution

show that HA gel is more effective in controlling inflammation, namely gingival bleeding and suppuration. The topical application of an HA-containing preparation represents a potentially useful adjunct in the therapy of gingivitis, although its use does not diminish the need for plaque reduction, as a primary therapeutic measure [10-12]. These results were in contradiction with the previous study carried out by Xu et al. who evaluated potential benefits of local subgingival application of HA gel adjunctive to SRP. They did not find any clinical or microbiological improvement by the adjunctive use of HA gel compared to SRP alone [13]. These contradictory results could be due to different inclusive criteria or different form of HA.

After mechanical therapy (SRP), probing depth reduction results from gingival recession and a gain of clinical attachment. In this study, gingival recession after multiple applications of HA gel after SRP, considerably improves, namely it decreases its values, while PD remains relatively stable. This means, the use of HA gel as an adjunct to SRP has multiple benefits on gingival parameters. Studies have documented reduction in the depth of gingival pockets along with a significant reduction in epithelial and lymphocyte cell proliferation with the use of HA gel [13-15].

Microbiologic analysis of periodontal pathogens has shown no significant differences for the two groups. HA gel seems not to have any antimicrobial effects on the bacterial species tested in this study. HA as a bactericidal agent is still controversial, but a study conducted by Pirnazar et al. suggested that HA in the Molecular Weight range of 1,300 kD may prove beneficial in minimizing bacterial contamination of surgical wounds when used in guided tissue regeneration surgery [16- 19].

Conclusions

It is obvious that HA gel improves clinical outcome of non-surgical therapy, especially gingival parameters. Thus, it has no antimicrobial effects, HA positively influences local inflammation. It proves to have a multifunctional role in the wound healing process after SRP. Hence, further long-term studies with better standards such as application time, quantity of application, different forms and concentration needs to be carried out for better understanding of therapeutic effect of HA in periodontal therapy.

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Manuscript received: 29.09.2016