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Clinical Evaluation of Hyaluronan Gel Alone or in Combination with Platelet- Rich Fibrin (PRF) in Periodontal Regenerative Surgery

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ABSTRACT

Purpose: This study was conducted to determine clinical effect of local application of hyaluronan gel alone or with platelet rich fibrin (PRF) in intrabony defects. **Material and Methods** sixteen patients with chronic periodontitis with twenty intrabony defects (probing depth ≥ 5 m m) were included in this study. Following scaling and root planing and re-evaluation, defects were divided to mucoperiosteal flap with 0.8 percent of hyaluronan gel (test) or platelet rich fibrin (test) or combination of both (test) or mucoperiosteal flap only (control). Clinical attachment level (CAL), probing pocket depth -for short- (PPD), gingival index (GI) and plaque index (PI) were taken at baseline,3 and 6 months. **Results:** clinical improvement was noticed statistically in each group through different intervals . nevertheless, non significant difference had been reported upon comparing different groups regarding percent change in GI,PPD and CAl. **Conclusion:** The local application of hyaluronan gel alone improve the clinical outcomes more than open flap debridment.However, hyaluronan gel with PRF in managing perio-dontal intrabony defects did not showed additional benefits.

KEYWORDS

Periodontal surgery,
Platelet rich fibrin,
Hyaluronic acid.

INTRODUCTION

One of the most common microbial infections in adults is periodontal disease. It is a disease that causes bacterial inflammation affecting tissues that support tooth [(1)] . The periodontium is affected by two popular diseases. The first disease is called Gingivitis which causes gingiva to be inflamed but does not result in loss of attachment and it

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is readily reversible by removal of etiologic factors and effective oral hygiene. While, the second disease is called periodontitis which not only causes inflammation of the gingiva but also causes inflammation of adjacent attachment apparatus and it can be characterized by both perio-dontal attachment and alveolar bone loss [2, 3].

A number of perio-dontal surgical procedures have been advocated. Pocket elimination procedures included gingivectomy and apically repositioned flap. On the other hand, pocket reduction and perio-dontal regeneration procedures included open flap technique and using the same technique (open flap) again plus bone grafts, guided tissue of periodontal regeneration (GTR) and combination of these modalities[4]. Various biological approaches have also been used to aid in developing of perio-dontal regeneration [5].

Particularly, hyaluronic acid (hyaluronan) has been found in all perio-dontal tissues. Hyaluronan is produced by enzymes of hyaluronan synthase (HAS) in different cells from the perio-dontal tissues[6]. Moreover**,** HA helps in perio-dontal regenerative procedures by maintaining spaces. HA may affect the functions of the cell that alter cellular and the extracellular environments. This may slow the penetration of microorganisms of perio-dontal diseases due to its viscoelastic property[7].

The influence of locally application of 0.8% hyaluronan gel with perio-dontal surgery was evaluated. Defects were divided to modified Widman flap surgery with 0.8% hyaluronan gel (test) or placebo gel (control) application. CAL and GR were reported with statistical significance changes in this research however PD, BOP and PI values were found to have statistical insignificance results [8].

Attempts were carried out to estimate the beneficial use of PRF in regeneration of IBDs and defects of furcation. In treating perio-dontal IBDs, several studies compared OFD in conjunction with the use of PRF versus OFD alone and followed up healing for 9 months. These studies demonstrate statistically significance enhancement in gain of CAL, IBDs fill measured and PPD. Also, less recession of marginal tissue was reported in (PRF) versus (ODF) sites [9, 10].

Since only few studies investigated the possibility of hyaluronan in perio-dontal wound healing alone or in combination with regenerative perio-dontal therapy. So this study had been executed to estimate clinically the effect of hyaluronan gel application alone or with PRF in perio-dontal regenerative therapy.

MATERIAL AND METHODS

Design of the study

This study was conducted on 16 patients chosen at random from the outpatient clinic in department of Oral Medicine, faculty of Dental Medicine for Girls, Al-Azhar University.

Sample Size

Sample size calculations achieved using http://biomath.info/power built on a previous study [8]. A total of 16 patients as a sample with 20 perio-dontal intrabony defects (5 in each of the four groups) will be sufficient to detect the difference. Total numbers of intrabony defects were randomly classified into 4 categories:

G I (Test group): mucoperiosteal flap along with 0.8 percent hyaluronan gel were used to treat 5 intrabony defects.

G II (Test group): mucoperiosteal flap with application of (PRF) alone used to treat 5 intrabony defects.

G III (Test group): five intrabony defects were treated with mucoperiosteal flap with combination of PRF and 0.8% hyaluronan gel.

G IV (Control group): five intrabony defects were treated with mucoperiosteal flap only.

The patients were selected according to selected criteria (free from any systemic disease, having moderate, advanced chronic periodontitis with at least one site with clinical attachment loss ≥ 5mm, non-smoker and non-pregnant women).

Pre-surgical therapy

Related therapy including scaling and root planning in addition to oral hygiene instructions was done for each patient. Then re-evaluation was done after 4 weeks.

Surgical protocol

Local anesthesia administration is followed by sulcular incisions of buccal, lingual and palatal types. Mucoperiosteal flaps were raised on the facial and lingual/palatal aspects of each involved site. Meticulous defect debridement of all inflammatory granulations tissue was performed .then root planning of The teeth using hand and ultrasonic instruments was done. The defect was filled by injection of HA gel using HA syringe with concentration 0.8% in group I. PRF plug was prepared and placed alone inside the defect with sterile tweezer and compressed inside defect with a condenser in group II .While in group III**,** PRF prepared and mixed with hyaluronan gel. Then placed inside the defect with sterile tweezer and compressed inside defect with a condenser. In group IV open flap debridement will be only carried out. Flaps were adjusted in its original place and sutured using Vicryl absorbable (4.0) sutures in figure eight suturing technique. Sutures were removed one week postoperatively. Antibiotics were described for 6 days after the surgery (Amoxicillin 500 mg 8hrs/7 days), 0.12% Chlorhexidine mouth washes were used to two weeks after the surgery twice per day[8]. Analgesic (Ibuprofen 600 mg tablets) was prescribed if needed.

Preparation of PRF

The technique introduced in 2001 [11] was used as a guide for PRF preparation. During the surgery, collection of 5ml intravenous blood from antecubital vein in a sterile 6ml vacutainer tube without anticoagulant was centrifuged in centrifugation machine at three thousands revolutions per minute (rpm) for ten minutes. In the middle of the tube, fibrin clot was formed. PRF was splitted from red corpuscles base using a tweezer, scissor after removal of ppp.

Clinical evaluation

The following clinical parameters were obtained for every patient at baseline, three months, six months postoperatively for the four groups:

Probing Pocket Depth (PPD)

Using Williams perio-dontal probe, The space from the gingival margin to the base of the pocket was measured.

Clinical attachment level (CAL)

CAL was calculated from the base of the pocket to cement-enamel junction.

Plaque Index (PI)

Amount of dental plaque was assessed according to Silness and Leo [12].

Gingival index (GI)

The patient's gingival condition was scored by measure of gingival index [11].

RESULTS

Clinical evaluation results:

Plaque Index (PI): In all studied groups, the results of the mean plaque index (PI) showed statistically significant decrease within the same group throughout the study period. However, the mean % change of PI showed a statistically significant difference at (baseline to 6 months) for all groups as in table (1).

Table (1): *Comparison of percent change (%) of plaque index (PI) between groups (Kruskall-Wallis test).*

PI percent change		(Mean)	Standard deviation	standard Error	95 percent Confidence Mean Intervals		Minimum	Maximum	P
					Lower Bound	Upper Bound			
First interval (Baseline to 3 months)	G. 1 (HA)	-36.67	41.50	18.56	-88.20	14.86	-100.00	.00	.935ns
	G. 2 (PRF)	-28.33	18.26	8.16	-51.00	-5.66	-50.00	.00	
	G. 3 (HA+PRF)	-21.67	21.73	9.72	-48.65	5.32	-50.00	.00	
	G. 4 (Control)	-25.00	25.00	11.18	-56.04	6.04	-50.00	.00	
Second interval (3months to 6 months)	G. 1 (HA)	-50.00	40.82	20.41	-114.96	14.96	-100.00	.00	.130ns
	G. 2 (PRF)	-73.33	25.28	11.30	-104.72	-41.95	-100.00	-50.00	
	G. 3 (HA+PRF)	-50.67	35.39	15.83	-94.61	-6.73	-100.00	.00	
	G. 4 (Control)	-26.67	25.28	11.30	-58.05	4.72	-50.00	.00	
Overall (Baseline to 6months)	G. 1 (HA)	-73.33[a]	25.28	11.30	-104.72	-41.95	-100.00	-50.00	
	G. 2 (PRF)	-81.67[a]	17.08	7.64	-102.87	-60.46	-100.00	-66.67	.034*
	G. 3 (HA+PRF)	-66.33[a, b]	20.43	9.13	-91.70	-40.97	-100.00	-50.00	
	G. 4 (Control)	-50.00[b]	.00	.00	-50.00	-50.00	-50.00	-50.00	

*Significance level p<0.05, *significant, ns=non- significant*

Gingival index (GI): In all studied groups the results of the mean gingival index (GI) revealed statistically significant decrease within the same group throughout the study period. Upon comparing the % change of GI for the four groups it is noted that there is no statistically significant difference throughout study period for all groups as in table (2).

Table (2): *Comparison of percent change (%) of gingival index (GI) between groups (Kruskall-Wallis test)*

PI percent change		(Mean)	Standard deviation	standard Error	95 percent Confidence Mean Intervals		Minimum	Maximum	P
					Lower Bound	Upper Bound			
First interval (Baseline to 3 months)	G. 1 (HA)	-12.35	21.65	9.68	-39.24	14.53	-50.00	.00	.164ns
	G. 2 (PRF)	-50.67	35.39	15.83	-94.61	-6.73	-100.00	.00	
	G.3 (HA+PRF)	-12.35	21.65	9.68	-39.24	14.53	-50.00	.00	
	G. 4 (Control)	-12.35	21.65	9.68	-39.24	14.53	-50.00	.00	
Second interval (3months to 6 months)	G. 1 (HA)	-14.00	21.91	9.80	-41.20	13.20	-50.00	.00	.375ns
	G. 2 (PRF)	-32.14	47.20	23.60	-107.25	42.96	-100.00	.00	
	G. 3 (HA+PRF)	-50.67	35.39	15.83	-94.61	-6.73	-100.00	.00	
	G. 4 (Control)	-36.67	41.50	18.56	-88.20	14.86	-100.00	.00	
Overall (Baseline to 6months)	G. 1 (HA)	-25.88	25.08	11.22	-57.02	5.26	-50.00	.00	.056ns
	G. 2 (PRF)	-73.33	25.28	11.30	-104.72	-41.95	-100.00	-50.00	
	G. 3 (HA+PRF)	-61.76	21.71	9.71	-88.72	-34.80	-100.00	-50.00	
	G. 4 (Control)	-48.24	35.57	15.91	-92.41	-4.06	-100.00	.00	

Significance level p<0.05, ns=non-significant.

Probing Pocket Depth (PPD): In all studied groups, results of the mean (PPD) revealed statistically significant decrease within the same group throughout the study period. Furthermore, on comparing the % change of PPD in all four groups it is noted that there is no statistical significance difference. The greatest reduction in PPD was reported in groupII (2.62 mm) followed by group I (3.24mm) then group IV (4.00mm) and finally group III (4.24) as in table (3).

Clinical attachment level (CAL): In all studied groups, the results of the mean Probing Pocket Depth (PPD) revealed statistically significant gain within the same group throughout the study period. When comparing the mean % change of CAL in all the four groups it is noted that there is no statistical significance difference as in table (4).

Table (3): *Comparison of percent change (%) of probing pocket depth (PPD) between groups (Kruskall-Wallis test)*

PI percent change		(Mean)	Standard deviation	Standard Error	95 percent Confidence Mean Intervals		Minimum	Maximum	P
					Lower Bound	Upper Bound			
First interval (Baseline to 3 months)	G. 1 (HA)	-37.58a	10.56	4.72	-50.70	-24.47	-50.00	-22.22	0.005*
	G. 2 (PRF)	-28.10 a, b	6.82	3.05	-36.56	-19.63	-33.33	-16.67	
	G. 3 (HA+PRF)	-2.86c	6.39	2.86	-10.79	5.08	-14.29	.00	
	G. 4 (Control)	-17.53b	12.14	5.43	-32.61	-2.45	-33.33	.00	
Second interval (3months to 6 months)	G. 1 (HA)	-22.30	18.28	8.17	-44.99	.39	-50.00	.00	0.211ns
	G. 2 (PRF)	-43.13	14.75	6.59	-61.44	-24.82	-60.00	-20.00	
	G. 3 (HA+PRF)	-25.38	9.69	4.34	-37.42	-13.34	-40.00	-16.67	
	G. 4 (Control)	-27.38	18.05	8.07	-49.80	-4.96	-50.00	.00	
Overall (Baseline to 6months)	G. 1 (HA)	-50.65	16.25	7.27	-70.83	-30.47	-75.00	-33.33	0.067ns
	G. 2 (PRF)	-58.51	14.80	6.62	-76.89	-40.13	-71.43	-33.33	
	G. 3 (HA+PRF)	-27.52	10.72	4.79	-40.83	-14.21	-40.00	-16.67	
	G. 4 (Control)	-38.46	24.13	10.79	-68.43	-8.50	-66.67	.00	

*Significance level p<0.05, * significant, ns=non-significant.*

Table (4): *Comparison for percent change (%) of clinical attachment level (CAL) between groups (Kruskall-Wallis test)*

PI percent change		(Mean)	Standard deviation	standard Error	95 percent Confidence Mean Intervals		Minimum	Maximum	P
					Lower Bound	Upper Bound			
First interval (Baseline to 3 months)	(HA)	-37.58[a]	10.56	4.72	-50.70	-24.47	-50.00	-22.22	0.005*
	(PRF)	-28.10 [a, b]	6.82	3.05	-36.56	-19.63	-33.33	-16.67	
	(HA+PRF)	-2.86[c]	6.39	2.86	-10.79	5.08	-14.29	.00	
	(Control)	-17.53[b]	12.14	5.43	-32.61	-2.45	-33.33	.00	
Second interval (3months to 6 months)	(HA)	-22.30	18.28	8.17	-44.99	.39	-50.00	.00	0.211ns
	(PRF)	-43.13	14.75	6.59	-61.44	-24.82	-60.00	-20.00	
	(HA+PRF)	-25.38	9.69	4.34	-37.42	-13.34	-40.00	-16.67	
	(Control)	-27.38	18.05	8.07	-49.80	-4.96	-50.00	.00	
Overall (Baseline to 6months)	(HA)	-50.65	16.25	7.27	-70.83	-30.47	-75.00	-33.33	0.067ns
	(PRF)	-58.51	14.80	6.62	-76.89	-40.13	-71.43	-33.33	
	(HA+PRF)	-27.52	10.72	4.79	-40.83	-14.21	-40.00	-16.67	
	(Control)	-38.46	24.13	10.79	-68.43	-8.50	-66.67	.00	

*Significance level p<0.05, * significant, ns=non-significant.*

DISCUSSION

The finale goal in periodontal therapy is regeneration of lost periodontal structures. Various techniques have been attempted to regenerate the lost perio-dontal tissues including open flap techniques with grafts of bone, guided periodontal tissue regeneration, various biological mediators such as growth factors, extracellular matrix proteins, the use of mediators of bone metabolism and applications of tissue engineering [4, 5] .

Thus, the study aimed to determine clinical influence of hyaluronan gel application alone or with (PRF) in intrabony defects in chronic periodontitis by measuring PI, GI, PPD and CAL.

There was a statistical significance reduction in plaque index and gingival index in all groups at three and six months versus baseline. This could be due to the proper scaling and root planning, the improvements in self performed oral hygiene measures as a result of participation in this study with perio-dontal examination scheduled monthly.

The results of this study demonstrated statistical significance reduction in PPD and significant gain in CAL at the end of the follow up period in all groups. PPD was achieved due to attachment gain and tissue regeneration. Moreover, this reduction may be due to the good adaptation of the flap following the surgery using the appropriate suturing technique.

In group I (HA alone), there were a statistical significance decrease in PPD and significant gain in CAL after 6 months. This could be attributed to the influence of H.A on promoting not only proliferation of cell but also migration then organization of granulation tissue. [12] Also, it speeds up regeneration of bone by chemotaxis, proliferation then sequential differentiation of mesenchymal cells [13].

In group II (PRF alone), there were a greater significant decrease in the PPD and a greater sig-

nificant gain in CAL after 6 months. Superior clinical results of this group may be due to the potential positive effect of PRF in healing process and regeneration. This could be attributed to a higher density of fibrin threads in PRF which provide additional steadiness to the wound and promote faster neo- angeogensis[11] .

In addition to the effect of PRF to stimulate the proliferation of human perio-dontal ligament fibroblasts [14]. Regarding bone regeneration, PRF increases osteoblast cell attachment, proliferation and collagen matrix synthesis by upregulating collagen related protein expression in human osteoblasts(Heat shock protein HSP 47 and lysyl oxidase (LOX)) [15,16].

In group III (HA +PRF), there were the least significant decrease in PPD and the least significant gain in CAL after 6 months. This may be due to controversial effect of hyaluronic acid on periodontal regeneration where, the contradiction may be attributed to the HA molecular weight, techniques of modification, concentration, inflammation presence and also cell kinds .it requires further investigations.

CONCLUSION

1. The use of hyaluronan gel alone showed superior results than its use with PRF
2. Using PRF alone in treatment of intrabony defects revealed the highest clinical outcomes.

REFERENCES

1. Beck J, Arbes SJ Epidemiology of gingival and periodontal diseases. In: Newman, MG; Takei, HH; Klokkevold, PR., editors. Carranza's clinical periodontology. St Louis: Saunders/Elsevier 2006; 2: 110-32.
2. The American Academy of Periodontology.Treatment of Plaque-Induced Gingivitis, Chronic Periodontitis, and Other Clinical Conditions. J Periodontol 2001 ; 72:1790-800.
3. Cortellini P, Tonetti MS . Regenerative periodontal therapy. In: Clinical periodontology and implant dentistry. 5th ed. Oxford 2008; 902–54.
4. Kaldahl WB, Kalkwarf KL, Patil KD, Dyer JK, Bates RE. Evaluation of four modalities of periodontal therapy. Mean probing depth, probing attachment level, and recession changes. J Periodontol 1988; 59:783-93.
5. Ijuin C, Ohno S, Tanimoto K, Honda K, Tanne K. Regulation of hyaluronan synthase gene expression in human periodontal ligament cells by tumour necrosis factor-alpha, interleukin-1beta and interferon-gamma. Arch Oral Biol 2001; 46:767–72.
6. Sutherland IW. Novel and established applications of microbial polysaccharides. Trends Biotechnol 1998; 16:41–6.
7. Fawzy El-Sayed KM, Dahaba MA, Aboul-Ela S, Darhous MS. Local application of hyaluronan gel in conjunction with periodontal surgery: A randomized controlled trial. Clin Oral Investig 2012; 16:1229–36.
8. Sharma A, Pradeep AR. Treatment of 3-wall intrabony defects in patients with chronic periodontitis with autologous platelet-rich fibrin: a randomized controlled clinical trial. J Periodontol 2011; 82:1705-12.
9. Sharma A, Pradeep A . Autologous platelet-rich fibrin in the treatment of mandibular degree II furcation defects: a randomized clinical trial. J Periodontol 2011; 82:1396-1403.
10. Dohan DM, Choukroun J, Diss A, Dohan S L, Dohan AJ, Mouhyi J, et al.. Platelet-rich fibrin (PRF): a second-generation platelet concentrate. Part I: technological concepts and evolution. Oral Surg, Oral Med, Oral Pathol, Oral Radiol, and Endod 2006; 101:37-44.
11. Loe H and Sillness J. periodontal disease in pregnancy. I. Prevalence and severity. ActaOdontol Scand 1963; 21: 533.
12. Parveen Dahiya, Reet Kamal.Hyaluronic Acid: A Boon in Periodontal Therapy. N Am J Med Sci 2013; 5: 309–15.
13. Bansal J, Kedige SD, Anand S.Hyaluronic acid: a promising mediator for periodontal regeneration. Indian J Dent Res. 2010; 21:575-78.
14. Tsai C-H, Shen S-Y, Zhao J-H, Chang Y-C . Platelet-rich fibrin modulates cell proliferation of human periodontally related cells in vitro. J Dental Sci 2009; 4:130-35.
15. Wu CL, Lee SS, Tsai CH, Lu K-H, Zhao J-H, Chang, Y-C. Platelet-rich fibrin increases cell attachment, proliferation and collagen-related protein expression of human osteoblasts. Aust Dental J 2012 ; 57:207-12.
16. Chang I, Tsai CH, Chang YC . Platelet-rich fibrin modulates the expression of extracellular signal-regulated protein kinase and osteoprotegerin in human osteoblasts. J Biomed Mater Res A 2010 ; 95:327-32.