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CLINICAL APPLICATION OF RADIESSE AND HYALURONIC ACID GEL FOR TREATMENT OF PAPILLAE DEFICIENCIES IN THE ESTHETIC ZONE

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ABSTRACT

Background: A black triangle or an open gingival embrasure is one of the main problems that compromise esthetics. Different surgical techniques have been utilized to resolve this problem. Consequently, minimally invasive techniques using filler injections have been recommended. Hyaluronic acid (HA), a naturally occurring polysaccharide; was widely used in treatment of deficient interdental papillae. On the other hand, Radiesse is calcium hydroxide dermal filler used in facial rejuvenation. This study was performed to compare the effect of Radiesse and hyaluronic acid gel in treatment of deficient interdental papillae.

Materials and Methods: A total of 30 female patients with 40 deficient interdental papillae were assigned into two groups A and B. Group A received hyaluronic acid gel injection while group B received Radiesse gel injection. Clinical data included papillary marginal gingival index, probing depth, clinical attachment loss, papilla presence index and height of interdental papilla. Data were taken at baseline, after three weeks, three and six months.

Results: Significant improvement occurred in both groups but this improvement was more prevalent in Radiesse group compared with HA group. There was a decline in the papillary height in the HA group after three and six months while in Radiesse group more long-lasting effect was denoted.

Conclusion: It was concluded that both fillers were biocompatible and safe for treatment of interdental papilla deficiency. Though, Radiesse gel was more effective and long-lasting compared with hyaluronic acid.

KEY WORDS: Hyaluronic acid, image J, interdental papilla, papilla presence index, Radiesse.

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INTRODUCTION

Esthetic awareness has improved massively in the last years. The ultimate goal in modern dentistry is to achieve "white" and "pink" esthetics in esthetically important zones. White esthetics refers to the natural dentition or the restoration of dental hard tissues with suitable esthetic materials. On the other hand, pink esthetics refers to the surrounding soft-tissues, which includes the gingiva and interdental papilla (IDP).^[1] A black triangle or an open gingival embrasure occurs as a result of deficiency or loss of papilla beneath the contact point which in turn greatly impede the esthetic results.^[2] Deficiency of interdental papilla causes not only an esthetic problem but also a functional impairment as it predisposes to food accumulation and the subsequent gingival and periodontal inflammation.[3]

The interdental papilla of the incisor region is usually pyramidal in shape. An ideal papilla will occupy the entire embrasure and will extend to the contact point, leaving no space in between the two adjacent teeth, thus not favoring food entrapment or being esthetically displeasing.^[4] Factors that favor the presence of an ideal interdental papilla are positive architecture of the underlying osseous support, thick rather than thin gingival biotype, and flat gingival scallop morphology with thin interproximal bone.^[5] In addition to square-shaped teeth with wide contact points rather than triangular teeth with narrow and more incisally positioned contact points.^[6,7] Also tooth brush trauma and decreased keratinization due to aging has been implicated as a causative factor of interdental papilla loss.[8]

Tarnow *et al.*^[9] proposed that the interdental papilla completely fills (100%) the space when the distance between the contact point and the crest of interdental bone is ≤ 5 mm. When the distance was 6 mm, the papilla was present 56% of the time, and when the distance was 7 mm or more, the papilla was present 27% of the time or less.

Cardaropoli *et al.*^[10] proposed the Papilla Presence Index (PPI). This index was based on esthetic evaluations; it measures interproximal soft tissue height in relation to the cementoenamel junction (CEJ), adjacent teeth, and the point corresponding to the ideal contact point.

Reconstruction of the lost interdental papilla is one of the most challenging esthetic problems. Nonsurgical approaches such as orthodontic, prosthetic, and restorative procedures were used to adjust the interproximal space, thereby inducing modifications to the soft tissues.^[11] Different surgical techniques^[12,13,14] have been anticipated to prevent or resolve the problem of black triangles including papilla preservation and papilla reconstruction. Papilla preservation techniques aim to restrict flap elevation in order to minimize the amount of bone resorption which in turn helps in preservation of interdental papilla. These techniques include papilla preservation flaps,^[15] modified papilla preservation flaps ^[16] and simplified papilla preservation flaps.^[17] On the other hand, papilla reconstruction techniques intended to recreate or to augment the lost papilla. Examples of these techniques are pedicle flap,^[18] semilunar coronally repositioned flap,^[19] envelop type flap,^[20] autogenous osseous and connective tissue grafts,^[21] bioabsorbable barrier membranes ^[22] and combined orthodontic-periodontal treatment.^[23,24] However, these techniques are all invasive and mostly unpredictable. Thus, minimally invasive techniques using filler injections have been proposed. Hyaluronic acid gel is one of these fillers widely used in augmentation of lost interdental papilla.

Hyaluronic acid (Hyaluronan; HA) is a naturally occurring linear polysaccharide of the extracellular matrix of connective tissue, synovial fluid, and other tissues. It possesses various physiological and structural functions.^[25] It is widely involved in tissue healing process by stimulating cell proliferation, migration and angiogenesis.^[26] HA is highly hydrophilic, when it contacts water, hydrogen bonding occurs between adjacent carboxyl and N-acetyl groups which enable HA to retain water and to form large concentrations that can occupy a large volume relative to its mass and to withstand compression.^[27] In addition, HA possessed no tissue or species specificity and induced minimal immunologic response and therefore have been considered as one of the safest substances available.^[28] Thus it has been recommended as dermal filler in treating some of the signs of aging.^[29] In the field of dentistry, HA has shown anti-inflammatory, anti-edematous, and anti-bacterial effects, hence; it was used in the treatment of periodontal disease.^[30] Besides. different studies [31,32] have demonstrated HA as an effective method to enhance deficient papillae.

Calcium hydroxylapatite (CaHA) fillers known as Radiesse are emerging semi-permanent dermal filler and were approved by Food and drug Administration (FDA) in 2006 as dermal and subcutaneous filler.^[33] It is composed of synthetically produced smooth uniform calcium hydroxide microspheres suspended in carboxymethylcellulose gel in ratio 30% microspheres to 70% gel by volume.^[34] Radiesse materials are biocompatible and possess low risk of stimulating immune response. It provides immediate and long-lasting volume enhancement.^[35] Thus, for many physicians, Radiesse is becoming the first choice for soft tissue augmentation.^[36]

The aim of the present study was to compare the effect of Radiesse and hyaluronic acid gel for treatment of deficient interdental papilla in the esthetic zone.

MATERIALS AND METHODS

Patient selection:

A total of 30 female patients were selected from the outpatient clinic of faculty of dentistry, Pharos University. The current study was conducted with approval from the Ethics Review Board of Faculty of Dentistry, Pharos University. All participants were provided with an overview of the clinical trial and a signed consent form was obtained from each participant. Among the selected patients, 20 patients had one deficient papilla between (11 and 21), while 10 patients each had two papillae deficiency between (11 and 21) and between (12 and 11) or (21 and 22). The contacting teeth were in close approximation. The contact areas were checked using dental floss that they were neither open nor too tight. Radiographic examination was performed and revealed no interdental bone loss. The alveolar crest between incisors appeared pointed and was located 1-2 mm below CEJ.

The inclusion criteria were:

- Age ranging from 25 to 35 years.
- Plaque index below 20%.^[37]
- Papillary marginal gingival index ^[38] is equal to zero.
- Normal probing depth (< 3 mm).^[39]
- Clinical attachment loss ^[40] ranging from zero to 2 mm.
- Respective teeth are free from caries with no fixed prosthesis or orthodontic appliance.

The exclusion criteria:

- · Patients with systemic disease
- Patients consuming drugs causing gingival hyperplasia
- Smokers, pregnant or lactating females.

Pre-operative phase

 Interdental papilla (IDP) height: Pre-operative photographs were taken perpendicular to teeth of interest using Nikon digital Camera D5300. A special, reproducible alignment device was used (Fig. 1). The device was used to take subsequent photos as close to the original photos as possible. A line was drawn at the midline of central incisor and was measured using a Microdent dental endodontic ruler to set the scale of the imageJ (Fig. 2). ImageJ 1.48v software program was used to measure the height of the selected papillae (Fig. 3).

- The Papilla Presence Index (PPI)^[10] scores were recorded at baseline:
 - *PPI 1:* When the papilla is completely present and coronally extends to the contact point to completely fill the embrasure. It is at same level of adjacent papilla.
 - **PPI 2:** Papilla is no longer completely present and lies apical to the contact point and not at the same level as the adjacent papillae, but the interproximal CEJ is still not visible.
 - **PPI 3:** Papilla is moved more apical and the interproximal CEJ becomes visible.
 - **PPI 4:** Papilla lies apical to both the interproximal CEJ and buccal CEJ.
- The Papillary Marginal Gingival Index (PMGI), Probing Depth (PD) and Clinical Attachment Loss (CAL) were recorded at baseline.

Drug application

- The selected papillae were randomly assigned into two test groups (A and B).
- For group A (HA group): After administration of a local anesthesia, a 23-gauge needle was used to inject less than 0.2 mL of a commercially available and FDA-approved HYALGAN^{®*} (hyaluronic acid gel) 2-3 mm apical to the coronal tip of the involved papillae of group A (Fig. 4).^[30]

- For group B (Radiesse group): 0.2 mL of a RADIESSE ^{®**}/LIDOCAINE^{***} blend was injected 2-3 mm apical to the coronal tip of the papillae (Fig. 5). The blending approach involved 0.2 mL of plain 2% lidocaine drawn into a 3mL syringe, and then attached to a 1.3 mL syringe of Radiesse through a Luer-lock connector. The Radiesse and lidocaine are pushed from one syringe to the other, back and forth 10 times to create a homogenous mixture.^[41]
- The patients were dismissed and requested not to brush their teeth at the day of injection and to resume oral hygiene measures on the following day by a soft-bristled toothbrush using Charter's technique ^[42] of tooth brushing at the anterior teeth. The patients were asked not to use dental floss at the treatment sites for 4 - 6 weeks and to use 0.12% chlorhexidine mouthwash.^[43]

Follow up

Photographs and follow up data including PMGI, PD, PPI, CAL, and IDP height were obtained at three weeks, three and six months later for all the respective areas.

Statistical analysis of the data

Data were fed to the computer and analyzed using IBM SPSS software package version 20.0. Student t-test was used to compare the two groups for normally distributed quantitative variables, ANOVA with repeated measures and Post Hoc test (LSD) were assessed for comparison between different periods. Mann Whitney test was used for comparing each two groups for ordinal variables, Wilcoxon signed ranks test was applied to compare between the different periods. Significance of the obtained results was judged at the 5% level.

^{*} HYALGAN® (Sodium Hyaluronate), Fidia Pharma, USA Inc.

^{**} RADIESSE® (calcium hydroxylapatite), MERZ AESTHETICS, USA.

^{***} LIDOCAINE HYDROCHLORIDE, Hospira, Inc., Lake Forest, IL 60045 USA



Fig. (1) Photographs were taken perpendicular to teeth of interest using a reproducible alignment device.



Fig. (2) A line at midline of the central incisor measured by a Microdent dental endo ruler



Fig. (3) IDP height measured by imageJ software program



Fig. (4) Hyaluronic acid gel application



Fig. (5) Radiesse/lidocaine application

RESULTS

A total of 40 papillae were assessed in the present study and were divided into two groups, group A received HA gel and group B received Radiesse/ lidocaine blend.

Table (1) presents the score of papilla marginal gingival index (PMGI) and papillary presence index (PPI). The PMGI was scored 0 (no inflammation) at baseline for both groups. For group A, all cases remained free from inflammation through the first three months. Though, after six months; two papillae showed mild inflammation (PMGI score 1).

Regarding group B, after three weeks one papilla showed mild inflammation (PMGI score 1) and two papillae with moderate inflammation (PMGI score 2). After three and six months only two papillae appeared with signs of mild inflammation (PMGI score 1). Concerning the PPI, 15 papillae out of 20 in group A showed marked improvement (PPI score 1) after three weeks, but this number was declined to 11 papillae and then to 10 papillae after three and six months respectively. On the other hand, 18 papilla in group B showed obvious improvement (PPI score 1) after three weeks. The number of improved papillae did not change after three months and was decreased to 17 after six months.

A comparison of the probing depth (PD), clinical

attachment loss (CAL) and PPI between the two studied groups at different follow up periods was shown in table (2). No significant difference existed between both groups at baseline for all parameters. Regarding the PD and CAL, no significant difference existed between both groups at three weeks, three and six months (for PD ^{MW}p = 0.432, 0.485, 0.485 respectively and for CAL ^{MW}p = 0.534 at the three follow up periods). While concerning the PPI, a significant difference existed within each group at three weeks, three and six months compared with baseline. Lower PPI scores were denoted in group B compared with group A at all follow up periods with significant difference at three and six months (^{MW}p = 0.014 and 0.018 respectively).

TABLE (1): Papilla	Marginal (Gingival inc	ex (PMG	() and	papilla	presence	index	(PPI) f	for the	two s	studied
groups.											

	Baseline	After 3 w.	After 3 m.	After 6 m.
PMGI				
Group A (n = 20)				
0	20 (100.0%)	20 (100.0%)	20 (100.0%)	18 (90.0%)
1	0 (0.0%)	0 (0.0%)	0 (0.0%)	2 (10.0%)
2	0 (0.0%)	0 (0.0%)	0 (0.0%)	0 (0.0%)
Group B (n = 20)				
0	20 (100.0%)	17 (85.0%)	18 (90.0%)	18 (90.0%)
1	0 (0.0%)	1 (5.0%)	2 (10.0%)	2 (10.0%)
2	0 (0.0%)	2 (10.0%)	0 (0.0%)	0 (0.0%)
РРІ				
Group A (n = 20)				
1	0 (0.0%)	15 (75.0%)	11 (55.0%)	10 (50.0%)
2	17 (85.0%)	5 (25.0%)	9 (45.0%)	9 (45.0%)
3	3 (15.0%)	0 (0.0%)	0 (0.0%)	1 (5.0%)
Group B (n = 20)				
1	0 (0.0%)	18 (90.0%)	18 (90.0%)	17 (85.0%)
2	16 (80.0%)	2 (10.0%)	2 (10.0%)	3 (15.0%)
3	4 (20.0%)	0 (0.0%)	0 (0.0%)	0 (0.0%)

	Baseline	After 3 w.	After 3 m.	After 6 m.
PD				
Group A (n = 20)				
Median (Min – Max.)	1.0(1.0-1.3)	1.0 (1.0-1.5)	1.0(1.0-1.5)	1.0(1.0-1.5)
Mean ± SD.	1.06±0.12	1.10±0.21	1.10±0.21	1.10±0.21
Group B (n = 20)				
Median (Min – Max.)	1.0(1.0-2.0)	1.0(1.0-2.0)	1.0(1.0-2.0)	1.0(1.0-2.0)
Mean ± SD.	1.05±0.22	1.08±0.24	1.10±0.31	1.10±0.31
мwр	0.317	0.432	0.485	0.485
CAL				
Group A (n = 20)				
Median (Min – Max.)	0.0(0.0-2.0)	0.0(0.0-1.5)	0.0(0.0-1.5)	0.0(0.0-2.0)
Mean ± SD.	0.20±0.52	0.13±0.39	0.13±0.39	0.15±0.49
Group B (n = 20)				
Median (Min – Max.)	0.0(0.0-2.0)	0.0(0.0-1.0)	0.0(0.0-1.0)	0.0(0.0-1.0)
Mean ± SD.	0.20±0.52	0.05±0.22	0.05±0.22	0.05±0.22
мwр	1.000	0.534	0.534	0.534
РРІ				
Group A (n = 20)				
Median (Min – Max.)	2.0 (2.0-3.0)	1.0(1.0-2.0)	1.0 (1.0-2.0)	1.5(1.0-3.0)
Mean ± SD.	2.15±0.37	1.25ª±0.44	1.45°±0.51	1.55°±0.60
Group B (n = 20)				
Median (Min – Max.)	2.0(2.0-3.0)	1.0(1.0-2.0)	1.0(1.0-2.0)	1.0(1.0-2.0)
Mean ± SD.	2.20±0.41	1.10ª±0.31	1.10ª±0.31	1.15ª±0.37
мwр	0.681	0.218	0.014*	0.018*

TABLE (2): Comparison between the two different groups regarding papillary presence index, probing depth and clinical attachment loss.

 ^{MW}p : p value for Mann Whitney test for comparing between the two studied groups

a: Significant with baseline

*: Statistically significant at $p \le 0.05$

Table (3) showed the height of the interdental papilla (IDP) measured by imageJ software program. At baseline no significant difference existed between both groups, the mean IDP height was 3.81 ± 0.49 for both groups. After three weeks a significant increase in the height of the IDP occurred in both groups. This increase was reduced for both groups after three and six months. Comparing both groups, the IDP height was significantly greater in group B than in group A at all follow up periods ('p < 0.001) (Fig. 6,7).

The percentage of change (increase) of the

IDP height from baseline to the different follow up periods was shown in table (4). The mean percentage of change for group A within the first three weeks was $13.3\% \pm 13.4$ which decreased to $12.9\% \pm 13.8$ and then to 7.9 $\% \pm 12.5$ after three and six months respectively. While for group B, the mean percentage of change was $35.3\% \pm 18.6$ after three weeks and only mild decrease occurred after three and six months (mean = $34.5\% \pm 18.6$ and 34.8 ± 18.6 respectively). The percentage of change was significantly higher in group B compared with group A (^{MW}p = 0.001) at the three follow up periods.

TABLE (3	3): Co	omparison	between	two	different	treatment	modalities	regarding	the IDI	P height

IDP height	Baseline	After 3 w.	After 3 m.	After 6 m.
Group A $(n = 20)$	3.81±0.49	4.31ª±0.67	4.28ª±0.64	4.10ª±0.59
Group B (n = 20)	3.81±0.49	5.12ª±0.40	5.09ª±0.43	5.10ª±0.43
^t p	0.897	<0.001*	<0.001*	<0.001*

*'p: p value for Student t-test for comparing between the two studied group a: Significant with baseline *: Statistically significant at p* ≤ 0.05

TABLE (4): Percentage of change of the IDP height from baseline to different follow up periods.

	% of change from baseline to						
IDP neight	After 3 w.	After 3 m.	After 6 m.				
Group A							
Median (Min. – Max.)	8.6(0.0-36.5)	4.5(0.0-38.1)	2.2(-0.7-37.8)				
Mean	13.3±13.4	12.9±13.8	7.9±12.5				
Group B							
Median (Min. – Max.)	30.3(0.2-82.6)	28.9(0.2 - 83.0)	28.9(0.2-83.0)				
Mean	35.3±18.6	34.5±18.6	34.8±18.6				
мwр	0.001*	0.001*	<0.001*				

^{MW}p: p value for Mann Whitney test for comparing between the two studied groups

*: Statistically significant at $p \le 0.05$



Fig. (6) A case of two interdental papilla reconstructions treated by Hyaluronic acid (HA) and Radiesse ® (R). A: at baseline, B: after 3 weeks, C: after 3 months, D: after 6 months.

Fig. (7) A case of two interdental papilla reconstructions treated by Hyaluronic acid (HA) and Radiesse ® (R). A: at baseline, B: after 3 weeks, C: after 3 months, D: after 6 months.

DISCUSSION

Interdental papilla reconstruction especially at the esthetic zone is amongst the most difficult periodontal treatments. Several surgical techniques have been proposed for papillary reconstruction.^[44] Examples of these invasive surgical methods are semilunar flap and connective tissue graft.^[45] Subsequently, minimal-invasive techniques including the injection of different fillers have been introduced to enhance esthetics in interdental papillae.^[18] HA has long been used as dermal filler ^[46,47] and also to augment deficient interdental papillae. Previous studies ^[19,48,49] demonstrated its positive effect in management of black triangles. On the other hand, Radiesse; a CaHA dermal filler offered encouraging results in the field of facial rejuvenation.^[50] Several studies ^[51,52,53] have confirmed its safety as a dermal filler but to the knowledge of the author it was not investigated as an interdental papilla filler.

The present study compares the effectiveness of HA and Radiesse filler materials in treatment of deficient papillae.

Radiesse was injected after being blended with lidocaine anesthetic. The FDA has approved in 2009 a protocol for mixing Radiesse with lidocaine.^[41] The addition of lidocaine to Radiesse has expressively reduced injection pain. Marmur et al.[54] concluded that Radiesse premixed with lidocaine resulted in significant pain reduction during filler injection while offering esthetic results comparable to that of Radiesse without lidocaine. In addition, the mixing protocol of Radiesse with lidocaine facilitates its extrusion from the needle than Radiesse alone.^[55] Furthermore, Sundaram et al.[56] showed that mixing Radiesse with lidocaine reduces the viscosity and elasticity of Radiesse. Likewise, Bussso and Voigts [57] reported that Radiesse/lidocaine blend represents the optimal protocol for preserving the viscoelastic properties without affecting the longevity of the clinical benefits of Radiesse.

Results of the current study showed that marked improvement occurred in both groups regarding the PPI scores and the IDP height. This improvement was significant at the three follow up periods compared with baseline. These results agree with Mansouri et al.^[58] who demonstrated that application of HA gel was successful for reconstruction of interdental papilla in the maxillary anterior region at six months follow up. Also, the results demonstrated that both fillers were safe. Though, Radiesse filler showed mild inflammation after three weeks in three patients while in the group treated by HA, inflammation was initially denoted in only two patients by the end of the study period (after six months). This can be attributed to the anti-inflammatory property of hyaluronic acid.^[59] Takahashi et al.^[60] reported that HA was able to inhibit interleukin-1 β . Moreover, Wang *et al*.^[61] demonstrated that HA down-regulates interleukin-8, inducible nitric oxide synthase and tumor necrosis factor alpha genes expression. On the other hand, previous studies [62,35] showed that the adverse effects of Radiesse included temporary inflammation with mild edema, erythema and pain.

In the present study, the papillae of both group showed no significant difference in PPI at baseline. Three weeks after treatment, group B (Radiesse) showed more normal papillae compared to group A (HA). By the end of this study (after six months), the number of normal papillae was reduced in group A compared with group B. Similarly, the results of IDP height measured by imageJ showed that Radiesse offered greater improvement after three weeks compared with HA. These results emphasized the superior effect of Radiesse as filler which agrees with Elson [63] and with Moers-Carpi et al.[64] Furthurmore, results showed that after six months the IDP height in group A was decreased by nearly 5%. While in group B, it remained nearly at the same level (reduced by only 0.6%) which confirms the long-lasting effect of Radiesse as filler. These results were in accordance with Moers-Carpi and Tufet [65] who concluded that CaHA demonstrated longer lasting results and greater improvement than HA. Similarly Jacovella et al.[66] reported that Radiesse was shown to be a highly effective, longlasting material for facial soft-tissue augmentation and that it can be considered a very good option for an aesthetic soft-tissue facial filler when real volumetric augmentation is needed.

CONCLUSION

From the current study we concluded that both HA gel and Radiesse gel were effective and safe for interdental papilla augmentation. Though, Radiesse gel offered more superior improvement concerning its immediate volumizing as well as its long-lasting effect.

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