The Scientific Temper (2023) Vol. 14 (3): 975-984

E-ISSN: 2231-6396, ISSN: 0976-8653

Doi: 10.58414/SCIENTIFICTEMPER.2023.14.3.64

https://scientifictemper.com/

REVIEW ARTICLE

Effect of hyaluronic acid application on gingival black triangles– A systematic review

Minas M. Ali[1], Fatema M. S. B. Nuhed[2], Ibtihal Ahmed M Alsheikhoon[3], Kholood K. S. Alhuthali[3], Ohood A. H. Almalki[3]

Abstract

Interdental papilla loss, also known as "black triangles," is a prevalent issue that both patients and dentists worry about. According to Singh and Vandana (2019a), the gingival black space is the loss of the papillary height. One of the most difficult periodontal issues to address is this one. According to V. P. Singh *et al.* (2013), tooth loss, incorrect restoration contouring, traumatizing oral hygiene practices, and dental spacing all play a role. Dentistry has paid a lot of attention to the use of hyaluronic acid (HA) injections for papilla regeneration in cases of interdental black triangles (BTs). The discussion here highlights the various strategies and results connected with employing HA injections for papilla regeneration.

Keywords: Gingival black triangles, Interdental papilla, Dentistry, Medical sciences.

Introduction

The loss of interdental papillas, often called "black triangles," is a common concern for dentists and patients. The gingival black space is the loss of the papillary height (S. Singh & Vandana, 2019a). It is one of the toughest periodontal problems to be treated. This is primarily due to the unique characteristics of interdental papillae, which include their small size, fragile location, and, most importantly, the limited blood supply, a major concern when performing any surgical procedure. Furthermore, black triangles are ranked as the third most disliked esthetic problem, as caries and apparent crown margins are to be considered the most (Abdelraouf, Dahab, Elbarbary, El-Din, and Mostafa, 2019). Open gingival embrasures result in several problems such as the retention of food debris, subsequently affecting periodontal health. Also, allowing air and saliva to pass through causes phonetic issues (S. Singh and Vandana, 2019a). Therefore, it's important to understand the etiology of BT to prevent their occurrence or treat them effectively.

Black triangle formation is a multifactorial defect. The etiology may involve one or several of the following factors: changes in papillary dimensional during orthodontic treatment (Rashid *et al.,* 2022), periodontal attachment loss leading to recession, alveolar bone height loss relative to the inter-proximal contact, embrasure height, root angulations, inter-proximal contact position, triangular-shaped crowns (Sharma & Park, 2010). Traumatic oral hygiene procedures, improper restoration contours, teeth spacing and tooth loss are contributing factors (V. P. Singh *et al.,* 2013). Black triangle formation resulting from the loss of the interdental papilla and bone is more prevalent in adults. Additionally, post-orthodontic treatment exhibiting BT are seen in 39 to 42 % of adolescent and adults (Sriphadungporn & Chamnannidiadha, 2017).

Absence of the papilla can be attributed to several factors. First, the availability of underlying osseous support. This emphasizes the significance of a positive architecture of the alveolar bone and pronounced gingival scalloping. Another important factor is the periodontal biotype, which can be categorized into two main groups: thin and thick. Friable and fragile features distinguish the thin periodontal biotype, thus, extra care during treatment is necessary to avoid recession. On the contrary, the thick biotype is fibrotic and resilient. Tooth morphology is another significant factor influencing black triangle formation. Teeth come in various forms, such as circular, square, or triangular, determining the gingival scalloping degree. The triangular

[1]General dentist, Qatar,

[2]Periodontal MSc student, Cairo University,

[3]General Dentist, Kingdom of Saudi Arabia

***Corresponding Author:** Author, Affiliation, E-Mail:

How to cite this article: Ali, M.M., Bin Nuhed, F.M.S., Alsheikhoon, I.A.M., Alhuthali, K.K.S., Almalki, O.A.H. (2023). Effect of hyaluronic acid application on gingival black triangles– A systematic review. The Scientific Temper, **14**(3): 975-984.

Doi: 10.58414/SCIENTIFICTEMPER.2023.14.3.64

Source of support: Nil

Conflict of interest: None.

Received: 08/07/2023 **Accepted:** 10/08/2023 **Published** : 25/09/2023

form is particularly challenging due to its divergent roots and thicker interproximal bone. Conversely, the square has a smaller interproximal distance from the osseous crest to the contact point which is more favorable. Additionally, the position of the contact point is important. The "5 mm rule," as studied by (Tarnow *et al.,* 1992), suggests that the space between the contact point and interproximal osseous crest should be 5 mm or less to allow the interdental papilla to fully fill the gingival embrasures (V. P. Singh *et al.,* 2013).

Various approaches exist for reconstructing lost interdental papilla or treating BT. Reconstruction can be achieved through surgical or nonsurgical methods. Several surgical modalities are available to prevent or treat BT formation. One such modality is papilla re-contouring, performed in the presence of localized gingival lesions that are treated with gingivectomy and free gingival grafts. The use of papillary re-contouring can prevent the development of BT after treatment. Another surgical method is the preservation of the papilla, achieved through restricted flap elevation. This approach minimizes bone resorption, aiding in preserving the interdental papilla. Lastly, papilla reconstruction requires the elimination of inflammation for success. Once inflammation is resolved different types of flaps can be employed (V. P. Singh *et al.,* 2013). Alternatively, nonsurgical aim to minimize the interdental papilla loss during dental treatments. These approaches can be carried out in various ways. For instance, placing contact points correctly during restorative or prosthodontic procedures helps preserve the embrasure space, ensuring an ideal papilla position (Ziahosseini *et al.,* 2014). Orthodontic treatment to close gingival embrasures is another method, where the direction of tooth movement and the labiolingual thickness of supporting bone and soft tissue are crucial for successful outcomes (Sharma & Park, 2010; Ziahosseini *et al.,* 2014). Papilla regeneration can be achieved through repetitive curettage of the destroyed papilla (Shapiro, 1985). Recently, HA has gained popularity for treating lost interdental papilla.

Without a doubt, black triangles occur in many patients, making their treatment a significant concern in modern dentistry. Numerous studies have demonstrated the success of HA in treating the loss of interdental papilla. Therefore, understanding this material's formation, pharmacology, mechanism, and indications is highly recommended. HA and modified HA find applications in medicine, including tissue engineering and drug delivery. HA is a natural linear polysaccharide that is biodegradable, biocompatible, and non-immunogenic. Furthermore, it is osteoconductive and, promotes angiogenesis and moderates' immune responses. Chemical modifications have been applied to HA through carboxyl and hydroxyl group functionalization, carried out in aqueous solutions (Park *et al.,* 2009). HA is a high molecular weight non-sulfated component of glycosaminoglycan, formed during various phases of the cell life cycle. It is an essential component of connective tissue, contributing to tissue hydrodynamics, cell migration, proliferation, tissue healing, repair properties, and reduced scar formation. Its physiological, structural, and biochemical properties provide tissue elasticity and stability, which are crucial for tissue regeneration (Sadat Mansouri *et al.,* 2013a). Additionally, it acts as a barrier to various gram-negative bacteria (Tanwar & Hungund, 2016a). Thus, HA is safe therefore, biocompatible, lacking evidence of cytotoxicity. HA is available in various forms and methods of application, such as creams, injections, or oral applications. However, patients with allergies to this material are not suitable candidates for HA use (Abdulhameed & Ibraheem, 2014).

Pharmacologically, HA present in tissues is mostly broken down by the bloodstream or lymphatic drainage. It is estimated to have a 20–30% turnover rate. In terms of pharmacokinetics, HA enters the bloodstream after breakdown and is subsequently removed by the liver. A small amount, about 2–10%, is excreted in urine. The plasma half-life of HA is 2–3 days, depending on its elimination process (Dahiya & Kamal, 2013).

Having understood HA as a material, focusing on its properties and applications is essential. HA possesses various beneficial properties for periodontal therapy. Periodontal therapy is performed to halt periodontal disease progression and restore missing periodontal support (Akizuki *et al.,* 2005). Firstly, it exhibits anti-inflammatory properties, which are highly valuable in treating periodontal disease. Moreover, HA is an antioxidant that scavenges oxygen-free radicals responsible for inflammation. It's important to note that a healthy periodontium's equilibrium between free radicals and antioxidants contributes to its mechanism. This suggests an inverse relationship between inflammation severity and antioxidant capacity, aiding in controlling the anti-inflammatory process during periodontal disease treatment (Dahiya & Kamal, 2013). A prior study reported the highly effective use of gel-form HA in reconstructing interdental papilla (Sadat Mansouri *et al.,* 2013b). Additionally, HA can serve as a scaffold for other molecules, including Bone Morphogenetic Protein-2 and Platelet-Derived Growth Factor-BB, used in directed bone regeneration and tissue engineering research (Tanwar & Hungund, 2016a). Consequently, HA demonstrates limitless potential in periodontal therapy, encompassing topical applications in subgingival regions to reduce microbial activity, bone regeneration, maintaining immediately inserted implants, treating peri-implantitis pocket, and gingival augmentation in mucogingival surgery. In cases of chronic periodontitis, HA use alongside scaling and root planning (SRP) has shown promise in reducing bleeding on probing (BOP), probing pocket depth (PPD), and clinical attachment level (Rajan *et al.,* 2014). Therefore, the application of Hyaluronic Acid in the mentioned cases has yielded promising results.

Materials and methods

Guidelines

This systematic review followed the updated preferred reporting items for systematic reviews and meta-analyses (PRISMA) (Moher *et al.,* 2009). This study complied with the ethical requirements as stated in the Declaration of Helsinki of scientific research. Accordingly, this research topic has been reviewed by the Institutional Review Board (IRB) Riyadh Elm University (REU) and approved with the IRB approval number FIRP/2020/ 78/266/259.

PICO Questions

The research question followed the patient/population, intervention, comparison and outcomes (PICO) framework. This study emphasized on 'How successful is HA in treating the loss of interdental papilla'.

Population: healthy Individual ≥ 12 years old with interdental space loss (black triangle).

Intervention: Hyaluronic acid application

Comparison/control: (1) number of HA applications (2) instructions after treatment

Outcomes.

Primary outcome: improvement of space closure by the use of HA after 3 and 6 months interval.

Secondary outcomes: patient satisfaction

Search Strategy and Eligibility Criteria

Two electronic databases (Medline via PubMed, and EMBASE via Ovid) were searched for relevant articles published up to March 2022. Combinations of MeSH search terms and text words were used: ("open embrasure *" OR "black triangle*" OR* gingival recession*") AND ("treatment*" OR "hyaluronic acid * dentistry" OR "papilla loss *") OR ("interdental papilla recession" OR "loss of interdental papilla).

The eligibility criteria include any gender that is ≥12 years of age and are exclusively healthy patients, exhibiting no periodontal diseases at the start of treatment. Additionally, all quantitative studies from 2010 onwards were only written in English. All manuscripts were included except *in-vitro* studies and studies done on animals.

Study Selection and Data Extraction

According to the eligibility criteria, a two-step screening procedure was performed. This process included the titles, abstracts, and full-text screening, all dependent on the eligibility criteria. If any missing or incomplete information were encountered, the publications were excluded.

Data Screening

Data includes authors' names and year of publication, participant age, method of treating black triangle, and study result. Changes in the interproximal papilla following HA application and patient satisfaction were also recorded.

Outcome Measures

The primary outcome measure was the improvement of space closure by using HA after 3- and 6-months interval whereas the secondary outcome was patient satisfaction.

Results

Selection of Studies

During the search process a total of 148 records were found. A total of 113 records remained after removing duplicates. Two reviewers screened the titles and abstracts, which resulted in the exclusion of 74 records. Reaching this phase, 39 articles were selected for full-text reading, which led to the exclusion of another 19 articles. The reasons of exclusions were; animal testing, *in-vitro* studies, and patients with systemic diseases. Finally, 20 articles fulfilled the eligibility criteria include, two case reports (Naorungroj, 2017; Tanwar & Hungund, 2016b); Two clinical trials on implants (Bertl *et al.,* 2017a; Spano *et al.,* 2020); Two having control groups by delivering saline in one group and other delivering HA (Abdelraouf, Dahab, Elbarbary, El-Din, & Zaki, 2019; Bertl *et al.,* 2017b) ; One comparing between different HA concentrations (S. Singh & Vandana, 2019b); Eight performing direct HA gel injection into the middle of the papilla(Awartani & Tatakis, 2016; Becker *et al.,* 2010; Lee, Seo, *et al.,* 2016; Ni *et al.,* 2019a; Pi *et al.,* 2017; Sadat Mansouri *et al.,* 2013a; Turgut Çankaya & Tamam, 2020; Yamada *et al.,* 2015); Two performing surgery in addition to injecting HA while Two compared the surgical approach vs surgical and HA injection, respectively (Guldener *et al.,* 2020; Kumar *et al.,* 2014; Lanzrein *et al.,* 2020; Pilloni *et al.,* 2019, 2018). All of these were then thoroughly analyzed for data extraction and answering the PICO question.

Study Populations

In both case reports (female patients aged 24 and 36) one was due to orthodontic relapse resulting in diastema, while the other complained of interdental papilla loss (Table 1). In the clinical trial performed on implants (one with 2 female adults with anterior implants and another with 3 female adults with maxillary implants and teeth) (Table 2). Two studies had control groups with one taking place around an implant-supported crown (Table 3). The studies discussed here present various methods for performing HA injections for papilla regeneration. Among the eight studies, different injection techniques such as direct injection above the mucogingival junction, injection directly in the attached gingiva beneath the missing papilla, and injection at the base of the papilla, have been employed (Table 4). Some studies have utilized a multi-step injection technique to achieve optimal results. The differences in injection sites, volumes,

Table 1: Case reports

Study year	*Population*	*Defect type*	*Main outcome*
(Naorungroj, 2017)	36 year old female	1.5 – 2 mm midline diastema due to relapse after orthodontic treatment, done to replace missing central incisors with lateral incisors	1-month follow-up after the last injection, ~1-mm black triangle space in the cervical region remained.
(Tanwar and Hungund, 2016b)	24 year old female	black triangle seen in the maxillary anterior region	Significant improvement of papillary volume and, hence, esthetic improvements after multiple use of HA.

Table 2: Clinical trials on implants

Study year	*Population*	*Defect type*	*Main outcome*
(Bertl *et al.,* 2017a)	2 adult females	Missing papilla in a single non-neighboring implant in the anterior maxilla.	Case 2: patient reported that within few hours after 2nd injection she has swollen lips and severe pain on the left side. After 3 days the symptoms subsided without any further intervention
(Spano *et al.,* 2020)	3 female adults	Anterior maxillary interdental papilla deficiencies adjacent to a tooth or a dental implant.	At 6 months: 1.75mm mean papilla fill. The VAS was used preoperatively and postoperatively to assess treatment success.

Table 3: Control Group

Study Year	*Population*	*Defect Type*	*Main outcome*
(Abdelraouf, Dahab, Elbarbary, El-Din, & Zaki, 2019)	10 patients, of which 3 males and 7 females between the age of 21–47, where equally divided into two group: placebo and HA	Deficient interdental papilla	Baseline to 6 months: HA group exhibited a statistically significant higher mean reduction than saline group.
(Bertl *et al.,* 2017b)	22 patients	A deficient papilla adjacent to an implant-supported crown in the anterior maxilla.	HA injection did not result in any noticeable clinical volume augmentation of deficient papillae.

Table 4: Direct HA injection

Study year	*Population*	*Defect type*	*Main outcome*
(Awartani & Tatakis, 2016)	9 of the average age of 36.4 years (range 22–55 years) have completed all study procedures and appointments.	Interdental papilla loss in 17 anterior sites (13 maxillary, 4 mandibular) 4 maxillary sites were classified as class II 13 sites (9 maxillary, 4 mandibular) were classified as class I.	4 and 6 months represent an average 62 and 41 % reduction in black triangle area, respectively.
(Becker *et al.,* 2010)	11 patients (7 females and 4 males). Average age 55.8 years old. Including 14 treated sites.	A minimum of one papillary deficiency in the esthetic zone. Two patients required treatment adjacent to teeth or implants for more than one site.	100% improvement were evident in three sites and eight had an improvement of 88–97%.
(Lee, Kim, *et al.,* 2016)	13 patients (6 males and 7 females) aged between 27–35 years	57 papillary deficiencies in the upper anterior area.	36 sites completed interdental papilla reconstruction, 21 sites showed an improvement range from 19–96%.
(Lee, Seo, *et al.,* 2016)	10 patients (4 male, 6 female) with age range of 27 to 35 years	43 papillary deficiencies in the maxillary anterior area.	A complete reconstruction of the papilla
(Ni *et al.,* 2019b)	8 females	Class I or II gingival papilla loss in anterior sites.	Patients with thick gingival biotype showed a better effect (increase in the height of the papilla & decrease of the black triangle.
(Sadat Mansouri *et al.,* 2013a)	11 patients (3 males and 8 females) with a mean age of 37.5 ± 14.4 years (range 22–61 years.	21 interdental papillae deficient sites in the maxillary anterior region sites: 16 in F and 5 in M no diastema nor spacing between teeth is present	It was found to be higher in younger patients (younger than 40). Significantly high Rate of interdental papilla reconstruction at the maxillary anterior region when compared to the baseline.

(Turgut Çankaya & Tamam, 2020)	20 patients	200 papilla deficient spaces	Irrespective of whether mandible or maxilla, the highest filling percentage was between the canine and lateral incisors. Noting that after 24 months most significant difference was between the central teeth.
(Yamada *et al.,* 2015)	Only case 2: 47-year-old woman	Papilla deficiency between the central incisors	The mean value of improved black triangle was 2.55 ± 0.89 mm. No significant difference by radiographic evaluation. Very high patients' satisfaction.

Table 5: Surgical intervention compound with HA application

Study year	*Population*	*Defect type*	*Main outcome*
(Guldener *et al.,* 2020)	12 healthy patients	One isolated mandibular miller class I or II gingival recession of a depth of ≥3 mm.	Predictable root coverage of isolated mandibular Miller Class I and II (Cairo Class 1) gingival recessions.
(Pilloni *et al.,* 2018, 2019)	30 healthy patients (14 females and 16 males) ranging in age from 21–47 years	Each patient had one gingival recession, if multiple recession seen then the deepest one was chosen, in case if all are in same level of recession the selection was performed by tossing a coin.	After 18 months of follow up There were no statistically significant differences in PPD in both groups on the other hand, the median recession reduction, CAL improvement and root coverage were statistically significantly different in both groups but much higher in the tested group.
(Kumar *et al.,* 2014)	10 patients (7 male and 3 females	20 sites having miller's class I gingival recession on the canine and premolar region	At 24 weeks, the change in RD was statistically significant ($P = 0.00$) in both groups and. The intergroup analysis, however failed to show statistical significance.
(Lanzrein *et al.,* 2020)	15 healthy patients	Multiple adjacent mandibular or maxillary RT1, RT2 of a depth of more or equal of 2 mm	Statistically significant root coverage was obtained in all 15 cases. Complete root coverage was obtained in 3 out of 15 cases

Table 6: Comparison between different HA concentration

Study (year)	*Population*	*Defect type*	*Main outcome*
(Tanwar & Hungund, 2016b)	10 systemically patients of both sets with age of 2540 years old	42 papillary recession defects but only 35 sits were followed up	Photograph analysis: All groups showed significant black space reduction Clinically: The 5% HA showed demonstrable enhancement of 41, 42.9 and 39.8% at 1, 3 and 6 months, respectively.

and intervals between injections are notable, which might contribute to variations in outcomes. Four reported a surgical approach in addition to HA application (one was about MCAT and LCT with HA, whereas the other was about MCAT or LCT with HA along with subepithelial palatal CT graft. While the other two compared CAF alone against CAF with HA. (Table 5). Additionally, one reported a comparison of different HA concentrations in a clinical application (Table 6).

Study Intervention

Several studies have investigated HA injections' use to regenerate the interdental papilla. In the case reports (Naorungroj, 2017) and (Tanwar and Hungund, 2016b) both applied HA injections in interdental papilla defects. An initial increase in the mesial emergence profile of centrals and mesiodistal of the laterals was exhibited in the (Naorungroj, 2017) report. Clinical trials on implants (Bertl *et al.,* 2017a)case 1 will be excluded due to the patient's medical condition since the patient is suffering from crohn's disease. On the other hand, case 2 and (Bertl *et al.,* 2017b, 2017a) (Awartani and Tatakis, 2016;) followed a 3-step technique firstly to create a reservoir directly above the mucogingival junction. Then, HA was injected into the attached gingiva, also 0.12 mL HA was injected apical to the tip of the papilla. The third step, is injecting 0.06 mL of HA 2 to 3 mm apical to tip of the papilla. (Spano *et al.,* 2020) had scaling for the interdental space and

adjacent teeth done. Then, a horizontal incision was carried out 2 mm apical to the mucogingival junction, creating a subperiosteal tunnel towards and under the deficient papilla and then 0.2 to 0.6 mL HA was administrated in the deficient area and the subperiosteal space. Cyanoacrylate was used as an adhesive. The studies that included a control group by delivering saline in one and HA in another (Abdelraouf *et al.,* 2019b) performed HA injections with phases of examination, re-evaluation, and injection. During the 3rd phase, 3 injections of 0.1 mm HA gel or saline solution were given at each papillary site. The needle was injected at a coronal direction 2 to 3 mm apical to the tip of the papilla and bevel was directed apically at a 45 angulation to the long axis of the tooth. The time interval was divided accordingly at baseline, 3- and 6-week interval. While, (Ni *et al.,* 2019b, 2019a) injected approximately 0.2 mL of cross-linked HA clear gel directly 2 to 3 mm apical to the tip of the papilla. Then, 1-minute gentle massage to the area was performed. This procedure was then repeated at 21 days (3 weeks) and then at 42 days (6 weeks). (Lee *et al.,* 2016b, 2016a) A one-pointed injection technique was used, to ensure the bevel of the needle pointing upwards and inserting it at a 45 angle 2–3mm apical to the papillary tip. 0.01mL of HA gel was injected at a 5-session interval of 0.02 mL each in each interdental papilla. This method is known to be the shooting method. Followed by light pressure application using gauze in the incisal direction for reconstruction. (Becker *et al.,* 2010; Sadat Mansouri *et al.,* 2013a) HA gel of less than 0.2 mL was injected at the affected sites 2-3mm apical to the coronal tip of papilla, then a 3 and 6-month follow-up was done and each was photographed for records. but if BT was still observed the procedure will be repeated again (max number of 3 times). Noting that (Becker *et al.,* 2010) had a control group who had saline injection. (Yamada *et al.,* 2015) discussed the many cases but they all lacked the use of HA but only the 2nd case performed papilla regeneration treatments with tissue-engineered papilla (TEP) with BMMSCs/PRP/HA complex were injected in BT of natural teeth. 5 comparison studies were done (Kumar *et al.,* 2014; Pilloni *et al.,* 2018, 2019); compared the CAF being done alone against CAF in conjunction with HA. While (Guldener *et al.,* 2020; Lanzrein *et al.,* 2020) studied the procedure of MCAT and LCT with HA, in addition to subepithelial connective tissue graft (SCTG).

Study Outcome

(Naorungroj, 2017): Had two follow-up visits, the first one was one month after the injection. 1mm of Papillary space remained in the cervical region. Therefore, the provisional crown and veneer contact area were modified and placed apically by flowable resin composite. The second visit was 1 month later, the final tooth preparation and impressions were done. Overall, patients were satisfied with the clinical result of the maxillary anterior teeth restorations. Despite the fact that a metal post shine compromised the esthetic result through effect and poor gingival contour.

A study done by a researcher had a significant increase in the papillary volume as well as remarkable esthetic improvements after multiple use of HA (Tanwar & Hungund, 2016b).

A study done by a researcher patient-reported she had adverse reactions like swollen lips and severe pain on the left side. However, these symptoms diminished after 3 days without any involvement (Bertl *et al.,* 2017a).

A study done by a researcher showed a mean of 1.75 mm of papillary fill was obtained after 6 months. The visual analog scale (VAS) assessed treatment success using pre and postoperative responses. Note that the long-term stability of papilla fill is unknown (Spano *et al.,* 2020).

A study done by a researcher in the comparison of results using three different methods (Abdelraouf, Dahab, Elbarbary, El-Din, & Zaki, 2019).

- Gender and BT Height: there was no significant difference in the interdental BT height between genders in both groups.
- **Time lapse and BT Height**
  - Three months after injections: HA group exhibited a statistically significant higher mean decrease in BT height compared to the control group.
  - Three to 6 Months: There was no statistically significant difference in BT height between the HA and control groups during this period.
  - Baseline to 6 months: The HA group demonstrated a statistically significant higher mean decrease in BT height compared to the saline group.
- **Surface Area of BT over time**
  - Baseline to 3 months: No statistically significant difference was observed in BT surface area changes between the HA and saline groups during this timeframe.
  - After 6 months: The HA group exhibited a statistically significant higher mean decrease in BT surface area compared to the saline group.

(Bertl *et al.,* 2017b) : The study's results were evaluated according to three main criteria:

- **Adverse Reactions (Pain Assessment)**
  - Test subjects experienced statistically significant discomfort during the first week after injection.
  - Discomfort during the second injection showed borderline significance.
- **Clinical and Radiographical Parameters**
  - Cases with a modified papilla index score (MPIS) of two maintained their scores throughout the treatment in both groups.
  - Baseline bleeding on probing (BOP) in the control group was significantly higher.
  - In the test group, BOP from baseline to three-month period was higher.
  - Black triangle (BT) area showed no significant differences over time in either group.

- **Esthetic Appearance**
  - The visual analog scale (VAS) technique was used to evaluate the esthetic appearance by both patients and examiners.
  - Overall, an acceptable appearance was observed at all assessment points.

A study done by a researcher had 62% BT area reduction during the baseline to four-month period. According to the patient's perspective, at four months of follow-up, 13 sites had a ≥50% reduction in BT area while two sites had complete papilla fill. on the other hand, at the 6 months period the sites were 8 and 3, respectively. The drawback of this procedure is the postoperative discomfort (Awartani and Tatakis, 2016).

A study done by a researcher patients had six to twenty-five months follow-up after the initial application of HA. Three sites exhibited a 100% improvement during this period, while eight sites showed 88- 97% improvement. Patient compliance highly influenced the number of visits (Becker *et al.,* 2010):.

A study done by a researcher complete interdental papilla reconstruction in 36 sites, whereas a range from 19 to 96% papilla improvement in twenty-one sites was evident. Although, (Lee *et al.,* 2016b) had complete papillary reconstruction after HA application (Lee *et al.,* 2016a).

A study done by a researcher stated that patients with thick gingival biotypes are prone to have enhanced results such as increased papillary height hence BT decrease (Ni *et al.,* 2019a).

A study done by a researcher compared the results according to three factors. Initially, patients of forty years or younger are found to have a higher association with papilla reconstruction. Then, a successful papillary reconstruction has been achieved at the sixth-month follow-up. Finally, the maxillary anterior region had a significant increase in the rate of papillary reconstruction when compared to the baseline. Hence, HA use can replace conventional invasive methods (Sadat Mansouri *et al.,* 2013a).

A study done by a researcher had significant enhancement at the 3, 12, and 24 months from the baseline. The enhancements were irrespective to whether the maxilla or mandible, yet the highest filling percentage was evident between canine and lateral incisors. Alternatively, comparing 24th month percentages between maxilla and mandible was mostly significant between the central incisors (Çankaya and Tamam, 2020).

A study done by a researcher no significant difference was evident while evaluating radiographically, yet it was seen to have a mean value of 2.55 ± 0.89 mm in black triangle improvement. Hence, patient satisfaction was extremely high without any adverse effects (Yamada *et al.,* 2015).

A study done by a researcher also had no postoperative bleeding, allergic reactions, abscess nor even loss of SCTG. Also, they had predictable root coverage for the isolated Miller class I and II (Cario class 1) gingival recession (Guldener *et al.,* 2020).

A study done by a researcher in the 18-month follow-up, neither group exhibited significant changes in probing pocket depth (PPD) or keratinized tissue (KT). Both groups experienced reduced swelling and discomfort. The median recession reduction (CAL) improvement and root coverage exhibited no significant differences amongst the groups, although the test group had slightly higher values (Pilloni *et al.,* 2019, 2018).

A study done by a researcher no statistically significant difference in PPD was observed in both groups. Nevertheless, both groups showed significant gain in the CAL. The experimental group achieved a higher percentage of root coverage (68.33 ± 28%) compared to the control group (± 30.22%). At the 24th week, root coverage change was statistically significant (P=0.00) in both groups. However, intergroup analysis failed to reveal any statistically significant differences (Kumar *et al.,* 2014).

A study done by a researcher the study showed significant root coverage in all fifteen cases. Three cases of which had complete coverage with an esthetic score of 10. Another three had >95%, four patients showed (90–95%), one with 87.5% finally, the last three showed 75, 77, and 64.6%, coverage, respectively. From the start till the follow-up period the mean keratinized tissue width increased from 2.5 ± 1.0 to 3.7 ± 0.7 mm (P < .0001). Yet, there was no statistical significance in probing depth (Lanzrein *et al.,* 2020).

A study done by a researcher clinically the groups that received the 1 and 5% showed a high significant improvement in papillary enhancement. The 5% exhibited a 41, 42.9, and 39.8% enhancement at 1, 3 and 6 months, respectively. Unfortunately, the 4% showed no clinical difference. However, the photograph analysis showed that the clinical reduction was to be significant (Singh and Vandana, 2019b).

The studies collectively contribute to understanding the effectiveness of HA in regenerating interdental papilla and addressing issues related to papilla deficiency in various clinical scenarios.

Outcome variables

Numerous clinical studies have investigated the efficacy of HA for interdental papilla regeneration, and they have employed various methodologies and postoperative instructions. Here's a summary of these studies and their approaches:

(Abdelraouf, Dahab, Elbarbary, El-Din, & Zaki, 2019; Awartani & Tatakis, 2016; Naorungroj, 2017; Sadat Mansouri *et al.,* 2013a; Tanwar & Hungund, 2016b)

These studies shared similar postoperative instructions, which included refraining from mechanical plaque control in the area for 24 hours, using a soft toothbrush with a roll

technique after the first 24 hours, avoiding dental floss at the treatment sites, using 0.12 or 0.2% chlorhexidine mouthwash twice daily for the first 2 weeks, and resuming routine oral hygiene after 2 weeks.

A study done by a researcher this study instructed patients to use ice packs for 3 hours post-surgery. Sutures were removed on the 7th day, then instructed to clean the site with 0.2% chlorhexidine twice daily for 10 days using a cotton pellet. Mechanical tooth cleaning with a soft toothbrush was resumed after 3 weeks. Noting that all the cases were examined and assessed for post-surgical adverse effects by the same examiner (Kumar *et al.,* 2014).

A study done by a researcher patients were instructed to stop tooth brushing, followed by the use of 0.12% chlorhexidine twice daily for the first 2 weeks. After suture removal, teeth brushing using a post-surgical soft toothbrush was advised (Pilloni *et al.,* 2018, 2019).

A study done by a researcher the same clinician conducted measurements, photography, VAS assessments, and surgeries (Spano *et al.,* 2020).

A study done by a researcher customized a stent for proper and standardized positioning of the probe at each measurement interval (Abdelraouf, Dahab, Elbarbary, El-Din, & Zaki, 2019).

A study done by a researcher instructed the patient to sit upright, with the Frankfurt plane plane parallel to the ground and the camera lens held horizontally. A formula was used (baseline area−postoperative area) × 100/baseline area, this was done to calculate the reduction percentage in the black triangle area (Awartani & Tatakis, 2016).

used computer software to assess the clinical photographic measurements.

A study done by a researcher Study models were created during the initial examination. These models were to standardize clinical photographic and radiographic measurements (Lee, Kim, *et al.,* 2016).

A study done by a researcher a computer program measured pixel changes between initial and final photographs (Becker *et al.,* 2010).

A study done by a researcher took photographs at the same distance horizontally and vertically after 3 weeks of the injection site. Similarly, (Tanwar & Hungund, 2016b) used images to compare the results (Sadat Mansouri *et al.,* 2013a).

A study done by a researcher scaling and root planning were performed at the treatment site and adjacent teeth (Yamada *et al.,* 2015).

A study done by a researcher examiners were assigned for unbiased evaluation; one examiner conducted all cases, while another administered HA gel injections. An occlusal stent was used at the injection site to have the measurements rounded to the nearest 0.5 mm. Patients were advised to start brushing coronal to the gingival margin using a soft brush and avoid flossing at the site (S. Singh & Vandana, 2019b).

A study done by a researcher have not mentioned any control variable (Bertl *et al.,* 2017b, 2017a; Guldener *et al.,* 2020; Lanzrein *et al.,* 2020; Ni *et al.,* 2019a).

Discussion

The use of HA injections for papilla regeneration in cases of interdental black triangles (BTs) has garnered significant attention in the field of dentistry. Several case reports, clinical trials, and comparison studies have investigated the efficacy of this technique in improving papillary fill and esthetics. The diverse range of methodologies and outcomes presented in these studies has led to a comprehensive discussion on the potential benefits that include a significant increase in the papillary volume as well as remarkable esthetic improvements after multiple use of HA, mean value of 2.55 ± 0.89 mm in black triangle improvement and patient satisfaction was extremely high without any adverse effects (Yamada *et al.,* 2015), both groups demonstrated significant CAL gain. There are some limitations and variations of HA injections for papilla regeneration. For instance, both groups demonstrated significant CAL gain with no significant PPD(Kumar *et al.,* 2014).

Conclusion

The discussion presented here underscores the diverse approaches and outcomes associated with using HA injections for papilla regeneration. While the studies collectively suggest that HA injections can lead to improved papillary fill and esthetics, variations in methodology, patient selection, and assessment methods can influence the results. Further research is necessary to establish the long-term stability of the outcomes, standardize injection techniques, and identify ideal patient candidates. Dentists should consider the available evidence, patient characteristics, and individual preferences when making clinical decisions regarding HA injections for papilla regeneration.

References

Abdelraouf, S. A., Dahab, O. A., Elbarbary, A., El-Din, A. M., & Mostafa, B. (2019). Assessment of hyaluronic acid gel injection in the reconstruction of interdental papilla: a randomized clinical trial. *Open Access Macedonian Journal of Medical Sciences*, *7*(11), 1834. https://doi.org/10.3889/oamjms.2019.478

Abdulhameed, B. S., & Ibraheem, L. (2014). Periodontal effect of 8% Hyaluronan as an Adjunct to Scaling and Root Planning in the Treatment of Chronic Periodontitis (Comparative Study). *J Dent Med Sci*, *13*, 76-81. https://doi.org/10.9790/0853-13837681

Akizuki, T., Oda, S., Komaki, M., Tsuchioka, H., Kawakatsu, N., Kikuchi, A., ... & Ishikawa, I. (2005). Application of periodontal ligament cell sheet for periodontal regeneration: a pilot study in beagle dogs. *Journal of periodontal research*, *40*(3), 245-251. https://doi.org/10.1111/j.1600-0765.2005.00799.x

Awartani, F. A., & Tatakis, D. N. (2016). Interdental papilla loss: treatment by hyaluronic acid gel injection: a case

series. *Clinical oral investigations*, *20*, 1775-1780. https://doi.org/10.1007/s00784-015-1677-z

Becker, W., Gabitov, I., Stepanov, M., Kois, J., Smidt, A., & Becker, B. E. (2010). Minimally invasive treatment for papillae deficiencies in the esthetic zone: a pilot study. *Clinical implant dentistry and related research*, *12*(1), 1-8. https://doi.org/10.1111/j.1708-8208.2009.00247.x

Bertl, K., Gotfredsen, K., Jensen, S. S., Bruckmann, C., & Stavropoulos, A. (2017). Adverse reaction after hyaluronan injection for minimally invasive papilla volume augmentation. A report on two cases. *Clinical oral implants research*, *28*(7), 871-876. https://doi.org/10.1111/clr.12892

Bertl, K., Gotfredsen, K., Jensen, S. S., Bruckmann, C., & Stavropoulos, A. (2017). Can hyaluronan injections augment deficient papillae at implant-supported crowns in the anterior maxilla? A randomized controlled clinical trial with 6 months follow-up. Clinical oral implants research, 28(9), 1054-1061. https://doi.org/10.1111/clr.12917

Çankaya, Z. T., & Tamam, E. (2020). An examination of the 2-year results obtained from hyaluronic acid filler injection for interdental papilla losses. *Quintessence International*, *51*(4), 274-284. https://doi.org/10.3290/j.qi.a43938

Dahiya, P., & Kamal, R. (2013). Hyaluronic acid: a boon in periodontal therapy. *North American journal of medical sciences*, *5*(5), 309. https://doi.org/10.4103/1947-2714.112473

Guldener, K., Lanzrein, C., Eliezer, M., Katsaros, C., Stähli, A., & Sculean, A. (2020). Treatment of single mandibular recessions with the modified coronally advanced tunnel or laterally closed tunnel, hyaluronic acid, and subepithelial connective tissue graft: a report of 12 cases. *Quintessence Int*, *51*(6), 456-463. https://doi.org/10.3290/j.qi.a44492

Lanzrein, C., Guldener, K., Imber, J. C., Katsaros, C., Stähli, A., & Sculean, A. (2020). Treatment of multiple adjacent recessions with the modified coronally advanced tunnel or laterally closed tunnel in conjunction with cross-linked hyaluronic acid and subepithelial connective tissue graft: a report of 15 cases. *Quintessence Int*, *51*(9), 710-719. https://doi.org/10.3290/j.qi.a44808

Lee, W. P., Kim, H. J., Yu, S. J., & Kim, B. O. (2016). Six month clinical evaluation of interdental papilla reconstruction with injectable hyaluronic acid gel using an image analysis system. *Journal of Esthetic and Restorative Dentistry*, *28*(4), 221-230. https://doi.org/10.1111/jerd.12216

Lee, W. P., Seo, Y. S., Kim, H. J., Yu, S. J., & Kim, B. O. (2016). The association between radiographic embrasure morphology and interdental papilla reconstruction using injectable hyaluronic acid gel. *Journal of periodontal & implant science*, *46*(4), 277-287. https://doi.org/10.5051/jpis.2016.46.4.277

Moher, D., Liberati, A., Tetzlaff, J., Altman, D. G., Altman, D., Antes, G., ... & Tugwell, P. (2009). Preferred reporting items for systematic reviews and meta-analyses: the PRISMA statement (Chinese edition). *Journal of Chinese Integrative Medicine*, *7*(9), 889-896. https://doi.org/10.1371/journal.pmed.1000097

Naorungroj, S. (2017). Esthetic reconstruction of diastema with adhesive tooth-colored restorations and hyaluronic acid fillers. Case reports in dentistry, 2017. https://doi.org/10.1155/2017/5670582

Ni, J., Shu, R., & Li, C. (2019). Efficacy evaluation of hyaluronic acid gel for the restoration of gingival interdental papilla defects. *Journal of Oral and Maxillofacial Surgery*, *77*(12), 2467-2474. https://doi.org/https://doi.org/10.1016/j.joms.2019.06.190

Park, J. K., Yeom, J., Oh, E. J., Reddy, M., Kim, J. Y., Cho, D. W., ... & Hahn, S. K. (2009). Guided bone regeneration by poly (lactic-co-glycolic acid) grafted hyaluronic acid bi-layer films for periodontal barrier applications. *Acta Biomaterialia*, *5*(9), 3394-3403. https://doi.org/10.1016/j.actbio.2009.05.019

Pilloni, A., Schmidlin, P. R., Sahrmann, P., Sculean, A., & Rojas, M. A. (2018). Correction to: Effectiveness of adjunctive hyaluronic acid application in coronally advanced flap in Miller class I single gingival recession sites: a randomized controlled clinical trial. *Clinical Oral Investigations*, *22*(8), 2961–2962. https://doi.org/10.1007/s00784-018-2567-y

Pilloni, A., Schmidlin, P. R., Sahrmann, P., Sculean, A., & Rojas, M. A. (2019). Effectiveness of adjunctive hyaluronic acid application in coronally advanced flap in Miller class I single gingival recession sites: a randomized controlled clinical trial. *Clinical oral investigations*, *23*, 1133-1141. https://doi.org/10.1007/s00784-018-2537-4

Pi, S., Choi, Y. J., Hwang, S., Lee, D. W., Yook, J. I., Kim, K. H., & Chung, C. J. (2017). Local injection of hyaluronic acid filler improves open gingival embrasure: validation through a rat model. *Journal of periodontology*, *88*(11), 1221-1230. https://doi.org/10.1902/jop.2017.170101

Rajan, P., Baramappa, R., Rao, N. M., Pavaluri, A. K., Indeevar, P., & Rahaman, S. M. U. (2014). Hyaluronic Acid as an adjunct to scaling and root planing in chronic periodontitis. A randomized clinical trail. *Journal of clinical and diagnostic research: JCDR*, *8*(12), ZC11. https://doi.org/10.7860/JCDR/2014/8848.5237

Rashid, Z. J., Gul, S. S., Shaikh, M. S., Abdulkareem, A. A., & Zafar, M. S. (2022, July). Incidence of gingival black triangles following treatment with fixed orthodontic appliance: a systematic review. In *Healthcare* (Vol. 10, No. 8, p. 1373). MDPI. https://doi.org/10.3390/healthcare10081373

Sadat Mansouri, S., Ghasemi, M., Salmani, Z., & Shams, N. (2013). Clinical application of hyaluronic acid gel for reconstruction of interdental papilla at the esthetic zone. *Journal of Iranian Dental Association*, *25*(3), 208-213.

Shapiro, A. (1985). Regeneration of interdental papillae using periodic curettage. *The International journal of periodontics & restorative dentistry*, *5*(5), 26-33.

Sharma, A. A., & Park, J. H. (2010). Esthetic considerations in interdental papilla: remediation and regeneration. *Journal of esthetic and restorative dentistry*, *22*(1), 18-28. https://doi.org/10.1111/j.1708-8240.2009.00307.x

Singh, S., & Vandana, K. L. (2019a). Use of different concentrations of hyaluronic acid in interdental papillary deficiency treatment: A clinical study. *Journal of Indian Society of Periodontology*, *23*(1), 35–41. https://doi.org/10.4103/jisp.jisp_332_18

Singh, S., & Vandana, K. L. (2019). Use of different concentrations of hyaluronic acid in interdental papillary deficiency treatment: A clinical study. *Journal of Indian Society of Periodontology*, *23*(1), 35. https://doi.org/10.4103/jisp.jisp_332_18

Singh, V. P., Uppoor, A. S., Nayak, D. G., & Shah, D. (2013). Black triangle dilemma and its management in esthetic dentistry. *Dental research journal*, *10*(3), 296. https://doi.org/10.4103/1735-3327.115129

Spano, S. J., Ghilzon, R., Lam, D. K., Goldberg, M. B., & Tenenbaum,

H. C. (2020). Subperiosteal Papilla Augmentation with a Non–Animal-Derived Hyaluronic Acid Overlay Technique. *Clinical advances in periodontics*, *10*(1), 4-9. https://doi.org/10.1002/cap.10075

Sriphadungporn, C., & Chamnannidiadha, N. (2017). Perception of smile esthetics by laypeople of different ages. *Progress in orthodontics*, *18*, 1-8. https://doi.org/10.1186/s40510-017-0162-4

Tanwar, J., & Hungund, S. A. (2016). Hyaluronic acid: Hope of light to black triangles. Journal of International Society of Preventive & Community Dentistry, 6(5), 497. https://doi.org/10.4103/2231-0762.192948

Tarnow, D. P., Magner, A. W., & Fletcher, P. (1992). The effect of the distance from the contact point to the crest of bone on the presence or absence of the interproximal dental papilla. *Journal of periodontology*, *63*(12), 995-996. https://doi.org/10.1902/jop.1992.63.12.995

Çankaya, Z. T., & Tamam, E. (2020). An examination of the 2-year results obtained from hyaluronic acid filler injection for interdental papilla losses. *Quintessence International*, *51*(4), 274-284. https://doi.org/10.3290/j.qi.a43938

Yamada, Y., Nakamura, S., Ueda, M., & Ito, K. (2015). Papilla regeneration by injectable stem cell therapy with regenerative medicine: long-term clinical prognosis. *Journal of tissue engineering and regenerative medicine*, *9*(3), 305-309. https://doi.org/10.1002/term.1737

Ziahosseini, P., Hussain, F., & Millar, B. J. (2014). Management of gingival black triangles. *British dental journal*, *217*(10), 559-563. https://doi.org/10.1038/sj.bdj.2014.1004