

Effects of Hyaluronic Acid Gel on Initial Wound Healing Following Tooth Extraction and Crown Lengthening Procedures: A Retrospective Analysis

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Aim: There is limited evidence highlighting the implications of adjunctive topical application of wound healing agents on clinical and patient-related outcomes in surgical procedures. The aim of the retrospective analysis was to evaluate the effects of 0.8% hyaluronic acid (HA) gel on wound healing following tooth extraction and crown lengthening procedures using the Inflammatory Proliferative and Remodeling (IPR) scale in a postgraduate clinical setting.

Methods: A retrospective assessment of medical record database related to clinical and patient-related outcomes of patients who received tooth extraction or crown lengthening procedures was conducted. Wound healing was assessed using the IPR scale providing scores for patient-reported postoperative pain, bleeding, granulation tissue, hematoma, tissue color compared to unaffected site, complete/incomplete flap closure, suppuration, and edema. The test group included participants who received an adjuvant application of 1mL of 0.8% HA gel *versus* control group participants receiving the same procedures without HA gel application.

Results: Overall, no statistically significant differences were observed between the total IPR wound healing scores for test (5.54 ± 1.02) *versus* control (5.19 ± 1.21 , $P=0.30$) groups. Bleeding and hematoma were less frequent in participants receiving 0.8% HA gel, though the differences were not statistically significant (bleeding: $P=0.09$, hematoma: $P=0.12$). Of the 45 participants analysed, 79.2% in the test group achieved successful inflammatory phase scores (5–8), compared to 76.2% in the control group ($P = 0.81$). More sites with a successful inflammatory phase (score 5–8) were observed in systemically healthy, male, non-smokers, and those with posterior mandibular surgeries, though without statistical significance.

Conclusion: Although 0.8% HA gel did not significantly improve early wound healing, well-designed clinical trials are necessary to evaluate its safety and potential benefits in routine periodontal surgeries. The IPR wound healing index demonstrated high reliability with excellent inter- and intra-examiner agreement in assessing the initial healing process after periodontal surgery.

Keywords: hyaluronic acid gel, wound healing, extractions, crown lengthening, periodontics

Introduction

The healing response is a physiological defense mechanism that aims to restore the integrity of damaged tissues after a surgical procedure. The nature of tissue disruption and wound closure conditions following periodontal surgery can influence the quality of wound healing.¹ Common periodontal therapies include a wide range of regenerative and resective procedures such as pocket reduction, access flaps, extraction of hopeless teeth, and crown lengthening procedures.²

The wound healing process following periodontal surgery consists of four overlapping phases: hemostasis and clot stabilization, inflammation (inflammatory phase), cell proliferation (proliferative phase), and wound remodeling and maturation phase.³ The immediate response after surgical injury includes clot formation and stabilization, following which, a cascade of inflammatory reactions occur within 5 to 6 hours wherein inflammatory cells, mainly polymorphonuclear neutrophils and monocytes, populate the clot.³ A proliferative phase initiates on the third day with granulation

tissue formation, that is rich in inflammatory cells, fibroblasts, and immature blood vessels,¹ transitioning into the remodeling phase for the maturation of the connective tissue and overlying epithelium.

Topical applications for enhancing intraoral wound healing typically focus on reducing inflammation, promoting cell proliferation, and accelerating tissue regeneration. Various topical treatments, such as adhesive tablets, gels, and films, have also been developed for oral wound healing.⁴ Hyaluronic acid (HA), is a high molecular weight material that occurs as a key component of the extracellular matrix and detected in secretions such as the gingival crevicular fluid, saliva, serum, as well as the mineralized and non-mineralized components of the periodontium.⁵ It is a non-sulfated glycosaminoglycan which aids in keeping the extracellular matrix hydrated and resilient.⁶ Within the periodontium, HA is produced by HA synthase enzymes in different cell types, including fibroblasts and keratinocytes in the gingiva and periodontal ligament, as well as cementoblasts and osteoblasts.⁷ Moreover, research also suggests that HA possesses bacteriostatic, fungistatic, anti-inflammatory, anti-edematous, osteoinductive, and pro-angiogenic properties.^{8,9} Due to its viscoelastic property and ability to absorb moisture from the surrounding environment, HA has been widely used in procedures requiring tissue repair and regeneration.¹⁰ While some studies have utilized 0.8% HA gel for treatment of intra-oral ulcers and lichen planus,¹¹ several studies have shown the significant role of HA in both surgical and non-surgical periodontal therapy with its potentials in stimulating cell migration, proliferation and differentiation, and promotion of angiogenesis, thereby accelerating wound healing.^{6,12} Moreover, animal studies evaluating the effect of HA on healing of extraction sockets in rats have demonstrated an increased and earlier deposition of trabecular bone in healing sockets with HA when compared to controls, suggesting that use of HA stimulates expression of osteogenic proteins, leading to accelerated healing.^{13,14} Routine application of these agents that may influence the patient's perception to pain and discomfort form an encouraging field of study. Tooth extraction and crown lengthening procedures are common surgical procedures performed in daily clinical practice. Crown lengthening procedures involve the removal of soft tissues with or without hard tissue manipulation. These procedures are necessary to expose sound tooth structure for proper placement of restorative margins without violating the supracrestal tissue attachment around the teeth.² The literature is sparse while evaluating the effects of HA gel application on wound healing in different surgical situations. This monitoring of wound healing following periodontal surgeries is an essential measure that allows clinicians to track progress and, when necessary, intervenes to ensure a favorable healing outcome.

For this purpose, several wound healing indices have been used in research and clinical practice, each with its own strengths and limitations, such as early wound healing index, Landry's healing index and its modification.^{15–19} However, some shortcomings related to its applicability have been encountered.¹ For example, clinical healing scores like Southampton Wound Scoring System or REEDA Scale tend to lack specificity in distinguishing wound healing between different healing phases.²⁰ Additionally, subjective interpretation based on visual assessment alone may not be able to differentiate between scar formation and true tissue regeneration and mainly focus on the percentage of physical closure of the wound rather than the quality of tissue regeneration.²¹ Alternatively, the Inflammatory Proliferative and Remodeling (IPR) scale has been proposed as a more objective tool.¹ The IPR scale is composed of three subscales corresponding to the three phases of healing that allow rating of each phase at its appropriate time point during the postoperative period.¹ Categorizing healing into distinct inflammatory, proliferative, and remodeling stages allows a clear, dynamic understanding of the wound's progress, thereby ensuring that incomplete or pathological healing (eg, chronic inflammation, fibrosis) is recognized early. The transcriptional changes that occur immediately after surgery continue during the inflammatory phase for up to 3–5 days. The inflammatory phase is considered the most important because inflammation can endanger the subsequent series of biologic events leading to early wound healing. The clinical and patient-related outcomes during this phase, particularly upon application of biologics, like 0.8% HA gel, have been sparsely reported in the literature. Therefore, the aim of this retrospective study was to evaluate the effects of using 0.8% HA gel on patient-related outcome measures, vis-à-vis, wound healing following tooth extraction and crown lengthening procedure, assessed by the IPR wound healing scale.

Materials and Methods

Participants and Data Acquisition

This is a retrospective assessment of medical records' data collected as a part of routine quality control of healthcare outcomes as established by the Quality Assurance and Professional Review Committee and approved by the ethical committee of the Mohammed Bin Rashid University – Institutional Review Board (MBRU IRB-2023-7). A waiver was signed to ensure patient confidentiality while providing access to the patients' medical records database and was conducted in accordance with the Declaration of Helsinki, as revised in 2013.²² The retrospective analysis followed the guidelines outlined in the STROBE (Strengthening the Reporting of Observational Studies in Epidemiology) checklist.²³

The data constituted medical records of patients who attended postgraduate periodontology dental practice and received surgical extraction of teeth or crown lengthening procedures between May 2022 and December 2023. The wound healing was assessed using the IPR scale (Table 1)¹ providing scores for each phase of wound healing. Potential participants were screened and selected based on the following inclusion and exclusion criteria:

Table 1 Characteristics, Timing, and Scoring of the IPR Wound Healing Scale

Score T/phase	Parameter	Score 0	Score 1	Total score
Inflammatory T: 3–5 days	Bleeding, spontaneously or on palpation	Yes	No	/8
	Granulation tissue	Yes	No	
	Hematoma	Yes	No	
	Tissue color	Redder or whiter than opposite side tissue	Like the opposite side tissue	
	Incision margins	Incomplete flap closure/ fibrin clot/partial necrosis/complete necrosis	Complete flap closure/fine fibrin line	
	Suppuration	Yes	No	
	Edema VAS (1–10)	VAS 6–10	VAS 1–5	
	Pain VAS (1–10)	VAS 6–10	VAS 1–5	
Proliferative T: 14 days	Re-epithelialization	Partial	Complete	/5
	Tissue color	Redder or whiter than the opposite side tissue	Like the opposite side tissue	
	Scar	Scar wider than 2mm/contour irregularity	No scar/ scar lesser than 2mm/ contour regularity	
	Suppuration	Yes	No	
	Pain VAS (1–10)	VAS 6–10	VAS 1–5	
Remodeling T: 6 weeks	Scar	Scar wider than 2mm/ contour irregularity	No scar/ scar lesser than 2mm/ contour regularity	/3
	Tissue color	Redder or whiter than the opposite side tissue	Like the opposite side tissue	
	Pain VAS (1–10)	VAS 6–10	VAS 1–5	
Total score				/16

Note: Reprinted from Hamzani Y, Chaushu G. Evaluation of early wound healing scales/indexes in oral surgery: a literature review. *Clin Implant Dent Relat Res*. 2018;20(6):1030–1035. © 2018 Wiley Periodicals, Inc.¹

Abbreviation: VAS, visual analog scale.

Inclusion Criteria

- Age ≥ 18 years; systemically healthy or mild disease controlled with medication – ASA I and II patients (according to the guidelines of the American Society of Anesthesiology).
- Patients who have undergone surgical extraction of unrestorable teeth or received functional crown lengthening procedure as a part of restorative treatment, with or without adjunctive use of 0.8% hyaluronic acid gel (Gengigel[®], Ricerfarma, Milano, Italy).
- Complete record of wound healing during the initial three to five days post-surgery, as assessed by the IPR scale.¹
- Signed informed consent at the time of surgical procedure.

Exclusion Criteria

- Missing or insufficient data.
- Uncontrolled systemic diseases (eg, diabetes mellitus with HbA1c $>7\%$, cardiovascular diseases, autoimmune disorders).
- Immunosuppressive conditions (eg, HIV/AIDS, organ transplant recipients).
- Bleeding disorders (eg, hemophilia, thrombocytopenia).
- Heavy smokers (>10 cigarettes per day).
- Bone metabolic disease and/or taking medications that affect bone metabolism.
- Long-term use of non-steroidal anti-inflammatory medications.

Clinical Parameters

Medical record database was evaluated and categorized into two groups: “test group” - sites receiving surgical extraction of unrestorable teeth or the ones that received functional crown lengthening procedure as a part of restorative treatment, with adjunct topical application of 0.8% HA gel post-surgery while the “control group” followed standard surgical protocols without HA gel. Demographic details including age, gender, health status, smoking status and details of surgical procedure from electronic health records were included and assessed by the primary authors (S.A. and M.S). The surgical procedures were performed following standardized clinical practice guidelines pertaining to anamnesis, aseptic protocol, pain management, and postoperative therapeutic care. All included participants’ data were primarily categorized, based on adjuvant application of 1mL 0.8% HA gel (0.8% hyaluronic acid periodontal gel (Gengigel[®] Prof, Ricerfarma, Milano, Italy)) after completion of extraction or crown lengthening procedure, as “test group”. Standardized application of prefilled 1mL syringes with plastic applicators tips provided by the manufacturer were used to dispense the gel at the approximating flaps of extraction site or the incision margins in case of crown lengthening procedures. The “control group” followed similar standard surgical protocols, without the adjunctive application of 0.8% HA gel. In order to avoid confounding when comparing the test versus control cohorts, clinical records were also checked to ensure no additional use of local hemostatic agents, tissue adhesives, surgical dressing, or periodontal pack at the site of surgical procedure.

Post Surgical Evaluation and Outcome Measures

Medical record database evaluating wound healing outcomes of patients who presented during the initial inflammatory phase (within the first 3–5 days) were recorded by the same examiners (S.A. and M.S). The inflammatory phase was assessed based on eight parameters. This began with the use of the visual analogue scale (VAS) to assess the post-operative pain as reported by the patient. The remaining parameters relied on the clinician’s expertise to evaluate bleeding (either spontaneous or upon palpation), the presence of granulation tissue formation, hematoma at the injury site, tissue color compared to the unaffected site, complete versus incomplete flap closure with potential partial or complete necrosis, suppuration, and edema (VAS scale) (Table 1). A score of 0 or 1 was assigned for each of the parameters; the inflammatory phase was considered “successful” when the score ranged between 5 and 8.^{1,24} The characteristics defining each parameter and scoring system are depicted in Table 1.

Source of Bias

The retrospective nature of the present study coincides with an increased risk of bias. To address misclassification and performance bias that might have occurred during therapy and post-surgical assessment, two authors (S.A. and M.S.) underwent a calibration phase in advance, consisting of repeated review of medical record database relevant to the study (inter-rater reliability of wound assessment using the IPR scale, kappa = 0.92) to assure consistent levels of assessment. Additionally, Intraclass correlation coefficient (ICC) involved assessing a total of 10 cases that were randomly selected and applicability of the scores (based on IPR classification) was assessed by two independent examiners (S.A. and M.S.) within a two-week interval to evaluate the reproducibility of the scores (ICC = 0.87, indicating a good agreement).

Sample Size Calculation

The determination of the sample size needed was based on adopting a significance level of 5% with 90% power using Gpower software, version 3.1.9.4.²⁵ The sample size calculation was also based on a previous prospective clinical trial that evaluated wound healing after wisdom tooth extraction and reported similar effect sizes.²⁴ A representative sample size of 50 participants were required to detect a mean difference of 1 and standard deviation of 0.8, and a significance level of 0.05 in cumulative scores of early wound healing (measured using the IPR wound healing scale), between the groups. To account for possible exclusions, a total of 60 participants were selected.

Statistical Analysis

The ICC and Cohen's kappa coefficient were used to measure intra- and inter-reproducibility of the scores, respectively, between the two examiners. Descriptive statistics (means, ranges, and standard deviations) were reported for the patients' demographic details within the two groups. Independent *t*-test was used to compare scores (based on the IPR wound healing scale) within the two groups. Statistical analysis was conducted through Statistical Package for Social Sciences SPSS (version 24.0, IBM for Mac). Significance for statistical analysis was set at $P < 0.05$.

Results

Demographic Characteristics

A total of 60 participants were enrolled in the study; however, 15 participants were excluded due to incomplete records of some of the assessed parameters leaving a total of 45 participants for final analysis. Due to the smaller-than-expected sample size, the study may have been underpowered to detect statistically significant differences between the test and control groups. The age of the participants ranged between 16 and 72 years with a mean age of 41.01 ± 12.64 years. Two age groups were broadly defined to cover young adulthood (<35 years old) and middle age/older adulthood (>35 years old). Almost half of the participants were females (46.7%) and ≤ 35 years old (42.2%). The majority of the participants were fit and healthy (ASA 1 status) and only 15.6% were light smokers. Surgical extractions accounted for 68.9% of the total procedures performed, while crown lengthening accounted for the remaining 31.1% with almost half of the procedures performed in posterior maxilla (44.4%). Both treatment and control groups were comparable with respect to demographics, surgical procedure and site (Table 2).

Inflammatory Wound Healing Score

The IPR score was recorded between the third- and fifth-day post-surgery to evaluate the inflammatory phase. The weighted Kappa values and ICC were 0.92 and 0.87, respectively, indicating substantial to almost perfect inter- and intra-examiner agreement. Table 3 displays comparisons of individual scores (test group *versus* control group) for the eight parameters that constitute the wound healing during the inflammatory phase (3–5 days). There were lesser incidents of bleeding and hematoma observed in participants receiving 0.8% HA gel compared with those in the control group. However, the differences between the two groups (bleeding: $P=0.09$, hematoma: $P=0.12$) were not statistically significant. With regard to evaluating the presence of suppuration, none of the surgical sites showed suppuration regardless of adjunctive HA application, while only four sites (2 in the test and 2 in the control group) demonstrated a pain VAS score of 6–10 (Table 3). Incomplete flap closure with the presence of fibrin clot and granulation tissue formation were also

Table 2 Characteristics of Participants and Sites

	Application of 0.8% HA gel (n = 24)	No wound healing agent (n = 21)	P-value
Gender (n) [†]			
Female	12	9	0.63
Male	12	12	
Age (years) [§]			
Mean (SD)	39.63 (13.71)	42.57 (11.27)	0.44
Age (n) [†]			
More than 35 years old	13	13	0.60
≤ 35 years old	11	8	
ASA physical status (n) [†]			
ASA I	18	18	0.37
ASA II	6	3	
Smoking habits (n) [†]			
Non-smokers	21	17	0.55
Smokers	3	4	
Surgical procedure (n) [†]			
Crown lengthening	8	6	0.73
Surgical extraction	16	15	
Surgical location (n) [†]			
Posterior maxilla	12	8	0.42
Posterior mandible	12	13	

Notes: [†]Chi-square test; [§]Independent t-test.

Abbreviations: ASA, American Society of Anesthesiologists; SD, standard deviation.

Table 3 Scores for Individual Parameters of Inflammatory Phase of IPR Wound Healing Scale

Parameter	Application of 0.8% HA gel (n = 24)	No wound healing agent (n = 21)	P-value
Bleeding (n) [†]			
Yes	3	7	0.09
No	21	14	
Granulation tissue (n) [†]			
Yes	15	15	0.53
No	9	6	
Hematoma (n) [†]			
Yes	0	2	0.12
No	24	19	
Tissue color (n) [†]			
Redder or white than opposite side tissue	17	16	0.69
Like the opposite side tissue	7	5	
Incision margins (n) [†]			
Incomplete flap closure / fibrin clot / partial necrosis / complete necrosis	22	17	0.29
Complete flap closure / fine fibrin line	2	4	

(Continued)

Table 3 (Continued).

Parameter	Application of 0.8% HA gel (n = 24)	No wound healing agent (n = 21)	P-value
Suppuration (n) [†]			
Yes	0	0	NA
No	24	21	
Edema VAS (n) [†]			
VAS 6–10	0	0	NA
VAS 1–5	24	21	
Pain VAS (n) [†]			
VAS 6–10	2	2	0.89
VAS 1–5	22	19	
Total score [§]			
Mean (SD)	5.54 (1.02)	5.19 (1.21)	0.30
Successful inflammatory phase (wound healing score of 5–8) (n) [†]			
Yes	19	16	0.81
No	5	5	

Notes: [†]Chi-square test. [§]Independent t-test.

Abbreviations: VAS, visual analogue scale; NA, not applicable.

detected based on two parameters in the IPR wound healing scale (Table 1). Regardless of the application of 0.8% HA gel, both groups exhibited a significantly higher prevalence of sites with granulation tissue formation. However, incomplete flap closure and the presence of a fibrin clot were also observed, reflecting the expected healing response associated with the surgical procedure under investigation. Overall, no statistically significant differences were observed between the total IPR scores for test (5.54 ± 1.02) versus control (5.19 ± 1.21 , $P=0.30$) groups based on the inflammatory wound healing score (Table 3). Furthermore, of the 45 participants analysed, 79.2% in the test group achieved successful inflammatory phase scores (5–8) compared to 76.2% in the control group ($P = 0.81$). (Table 3). Generally, more sites with successful inflammatory phase (score of 5–8) were recorded, in participants who were systemically healthy, males, non-smoker and had surgical procedures conducted in posterior mandible, although statistically insignificant (Table 4, Figure 1). Thus, none of the demographic characteristics – participant gender, age, systemic health, smoking status

Table 4 Successful Inflammatory Phase (Score of 5–8) by Participant- and Site-Related Factors

	Score of 5–8 (n = 35)	Score < 5 (n = 10)	P-value
Gender (n)			
Female	15	6	0.34
Male	20	4	
Age (years) [§]			
Mean (SD)	40.23 (12.47)	43.70 (13.24)	0.45
Age (n) [†]			
More than 35 years old	19	7	0.38
≤ 35 years old	16	3	

(Continued)

Table 4 (Continued).

	Score of 5–8 (n = 35)	Score < 5 (n = 10)	P-value
ASA physical status (n) [†]			
ASA I	27	9	0.37
ASA II	8	1	
Smoking habits (n) [†]			
Non-smokers	30	8	0.66
Smokers	5	2	
Surgical procedure (n) [†]			
Crown lengthening	11	3	0.93
Surgical extraction	24	7	
Surgical location (n) [†]			
Posterior maxilla	16	4	0.75
Posterior mandible	19	6	

Notes: [†]Chi-square test. [§]Independent t-test.

Abbreviations: ASA, American Society of Anesthesiologists; SD, standard deviation.

(only light smokers were included in the study) and site-related factors – location and type of surgical procedure influence any significant impact on the IPR score (Table 4, Figure 1).

Additionally, similar “successful inflammatory phase” scores ranging from 5 to 8 were observed, irrespective of the type of surgical procedure administered (extractions versus resective crown lengthening procedures); likewise, although the adjunctive topical application of 0.8% HA gel in the test group showed a slightly higher proportion of successful

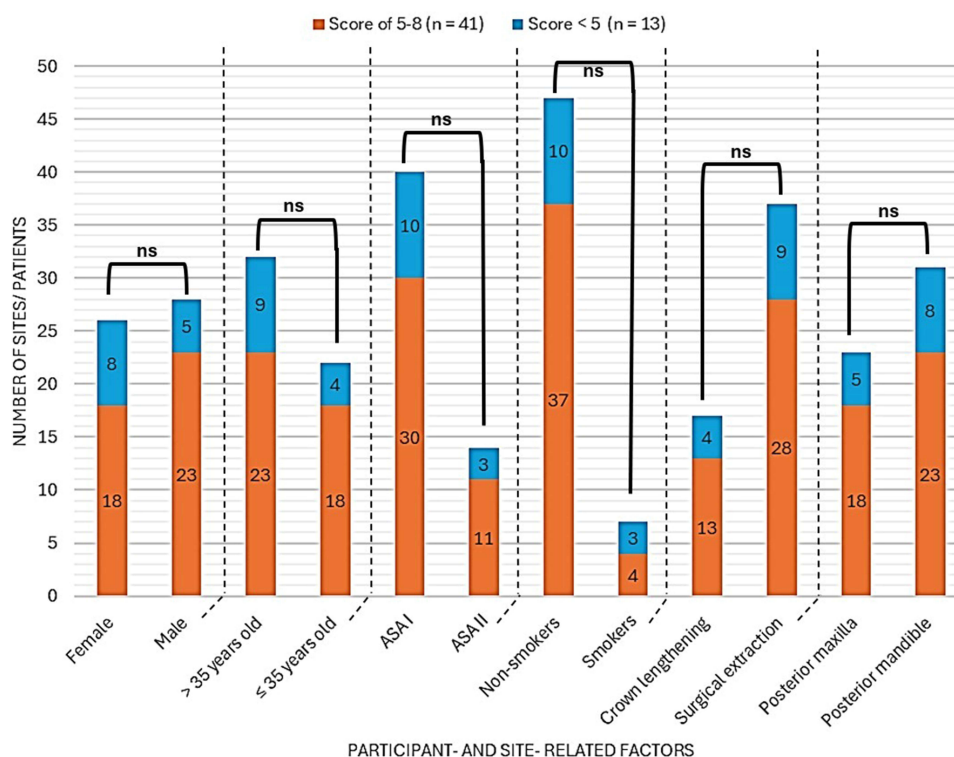


Figure 1 Successful inflammatory phase (score of 5–8) by participant- and site-related factors ($P > 0.05$).

Abbreviation: ns, non-significant.

healing outcomes, the difference was not statistically significant ($P = 0.81$), suggesting limited benefits of 0.8% HA gel during the inflammatory phase (Table 3). While efforts were made to account for potential exclusions, unforeseen factors such as participant dropout contributed to the reduced sample size than anticipated. The reduced statistical power may have limited the ability to detect small but clinically relevant effects.

Discussion

The primary objective of this retrospective analysis was to evaluate the effect of topical application of 0.8% HA gel on initial wound healing post extraction and crown lengthening surgical procedures. This study focused on comparing clinical and patient-related outcomes during the inflammatory phase of healing (3–5 days) based on the IPR wound healing scale.¹ The eight parameters that constitute the inflammatory phase involve multiple site-specific variables – bleeding, hematoma, presence or absence of granulation tissue *versus* complete wound closure, partial *versus* complete necrosis of the surgical site. Although participants receiving 0.8% HA gel showed lower incidence of bleeding and hematoma compared with those that did not receive any adjunctive wound healing agent, the differences might be clinically relevant, however, were not statistically significant. Interestingly, other key findings of this study also identified sites with successful inflammatory phase (score of 5–8), mainly in participants who were healthy males, aged >35 years old, non-smoker and received surgical extractions in posterior mandible.

In contrast to findings from this study, a significant positive effect of intrasocket application of HA gel on wound healing following extraction of impacted mandibular third molars has been demonstrated in a recent clinical trial.²⁶ That study showed that the application of 1% HA gel can be significantly effective in reducing postoperative pain, edema, and trismus on the first, third, and seventh postoperative day following surgery. Another study has also advocated introduction of 1% hyaluronic gel with a gelatin sponge, to be more beneficial in preventing post-extraction complications such as “dry socket”.²⁷ The discrepancies in findings may be attributed to various factors like differences in concentration of HA gel, along with scaffold that may have prevented a “wash-out” effect intraorally, study design (prospective clinical trial *versus* retrospective interpretation of medical records database), and lack of larger sample size.

Our results, however, remain comparable to those showcased by Yahya et al (2021), wherein, the IPR scale was used to monitor wound healing after surgical extraction of wisdom teeth, demonstrating lower scores for females compared to male participants (6.18 ± 1.33 and 4.56 ± 0.97 , respectively).²⁴ Similarly, our findings align with Yahya et al, where minimal additional benefits of HA gel in early wound healing were observed.²⁴ However, other research highlights its potential in reducing postoperative complications, such as pain and edema, particularly with higher concentrations (1%) or alternative application techniques.²⁷

Furthermore, granulation tissue formation, redness of healing tissues, edema and incomplete flap closure with the presence of fibrin clot, in this study, were observed in the majority of the surgical sites within the first 3–5 days of follow-up, regardless of the use of 0.8% HA gel. These findings correspond to another study by Yildirim et al (2018), where tissue color match, in sites where HA gel was applied, was only observed after connective tissue maturation at 21 days post-surgery.²⁸ This may indicate minimal influence of HA gel during the early inflammatory phase with need for longer follow-up period to identify any impact of HA gel on the proliferative as well as remodeling phases.

While several studies evaluated the use of HA gel as an adjuvant to non-surgical periodontal therapy, with minimal to no additional benefits in clinical or microbiological outcomes, the authors identified scarce data that evaluated patient-related outcome measures (PROMs) with HA gel after resective periodontal surgical procedures.²⁹ One such randomized controlled trial compared the clinical and radiographic efficacy of 0.8% HA gel as an adjunct to open flap debridement (OFD) in treatment of periodontitis (stage II or III) presenting with intrabony defects.³⁰ There were significantly better periodontal outcomes in terms of clinical attachment level gain and defect bone fill in patients receiving HA gel in conjunction with OFD at the end of twelve months. Similar positive results with the local application of HA gel as an adjunct to modified Widman flap surgery in the treatment of chronic periodontitis have also been noted.³¹ While the aforementioned studies evaluated clinical and radiographic parameters, they lacked focus on identifying PROMs related findings. Moreover, the application of HA gel has also been associated with decreased incidence of developing post-surgical infections due to its ability to reduce bacterial contamination of the wound site.⁹ While none of the healing sites in our study had suppuration within the first 3–5 days, only four sites had pain scores of more than 5 (based on VAS

scale) in patients with or without the application of 0.8% HA gel. Overall, a statistically significant difference between the test and control group was not detected in any of the parameters of the inflammatory wound healing score, regardless of the surgical procedure. Moreover, while differences in surgical protocols for extractions *versus* crown lengthening procedures exist, these differences in severity/complexity of the surgical procedure did not affect the inflammatory phase, implying that other factors affecting tissue management, such as tissue margins approximation and complete flap closure using sutures may significantly influence early wound healing process. Further, differences in factors such as surgical approach, precision, and post-operative care might lead to variations in tissue healing and recovery times. Even with standardized protocols, individual clinician expertise and the surgical technique implemented, can contribute to differences in outcomes. It is important to recognize that these procedural variations, while accounted for to some extent in the study design, could still impact the overall results and should be considered when interpreting the findings. Interestingly, recent systematic review has also highlighted the combination of ozone therapy and HA's therapeutic potential in acute or chronic oral inflammatory conditions.³² The findings suggest that the combined application of topical HA and ozone therapy is highly effective in enhancing post-operative healing after dental procedures while also yielding beneficial outcomes with chronic gingivitis, periodontal inflammation, and oral ulcers.³²

The IPR scale utilized in the current study attempted to address the shortcomings of the other wound healing scales. It is a comprehensive instrument formulated to provide scores for each of the three healing phases, based on a combination of subjective assessment by the patient (VAS for pain and edema) and objective evaluation of the surgical site by the clinician. Our study primarily focused only on the eight parameters related to the initial inflammatory phase, as HA gel pertains to affect the molecular mechanisms associated with the changes that occur in the first 3 to 5 days post injury. Hamzani et al (2018) justified the increased weightage for the inflammatory phase in the final score on the basis that any impairment during the early wound repair can have cascading effects on the entire series of biologic events. The remodeling phase (not applied in our study) carried the lowest weightage as this phase can continue to evolve over several years based on the equilibrium between matrix degradation and formation. While the scale has been previously used in sites that received extractions, no comparative data existed on the use of the IPR scale to evaluate wound healing response across different surgical techniques, this retrospective analysis, within its limitations, attempted to address them.

The present study has several limitations related mainly to the retrospective design and reliance on medical records which may have introduced selection and measurement bias. More importantly, participant dropout contributed to the reduced sample size than anticipated, that may have limited the ability to detect small but clinically relevant effects. Additionally, variability in surgical techniques among clinicians could have influenced outcomes. Nevertheless, the study provides a framework to design future prospective randomized controlled trials to estimate the effect of introducing 0.8% HA gel after surgical periodontal procedures.

Conclusion

While 0.8% HA gel did not significantly enhance early wound healing, its safety profile and potential to reduce postoperative complications warrant further investigation. Further well-designed clinical trials are necessary to assess the benefits of the adjunctive use of 0.8% HA gel on wound healing following routine periodontal surgeries, particularly during the early phase of wound healing. Moreover, the IPR wound healing index was proven to be a reliable tool with superior inter- and intra-examiner agreement in assessing initial healing process after periodontal surgical procedures.

Disclosure

The authors report no conflicts of interest in this work.

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