

Original article

Topical Hyaluronic Acid Gel as an Adjunct to Surgical Gingival Depigmentation: A Pilot Clinical Study on Early Wound Healing and Postoperative Pain

Abrar Ajali^{ID}, Abduladeem Gadad^{ID}, Gofran Aboushmkh^{ID}, Aisha Balha^{ID}, Fatima Kosibat^{ID}, Ansam Aldali^{ID}, Reham Elghawi^{ID}

Department of Periodontology, Faculty of Dentistry, Attahadi University, Tripoli, Libya

Corresponding Email. abdo.figo@yahoo.com

Keywords:

Hyaluronic Acid, Gingival Depigmentation, Wound Healing, Postoperative Pain, Periodontology

ABSTRACT

Gingival depigmentation is a common cosmetic periodontal procedure that heals by secondary intention, making postoperative pain and early wound healing important clinical concerns. Hyaluronic acid (HA), a naturally occurring extracellular matrix component with anti-inflammatory, angiogenic, and wound-healing properties, may be useful as an adjunct to periodontal surgery. This study assessed topical HA gel after surgical gingival depigmentation. Fifty patients with gingival hyperpigmentation were allocated equally to an HA group (n=25) and a non-HA control group (n=25). Standardised healing indices and a visual analogue scale were used to assess early healing and postoperative pain. By day 7, clinically assessed pigmentation reduction from baseline DOPI was 97.2% in the HA group versus 76.8% in controls ($p<0.001$), and complete pigmentation resolution (DOPI=0) occurred in 92% versus 48%, respectively. Mean epithelialisation time was reduced by 2.5 days (30% faster; $p<0.001$). Pain on days 3 and 7, erythema, and oedema were lower with HA; patient satisfaction was higher, and no adverse events were reported in the HA group. These findings support topical HA as a promising adjunct following gingival depigmentation, while larger controlled studies with standardised protocols and longer follow-up are warranted.

Introduction

Gingival depigmentation is a periodontal esthetic procedure that removes melanin pigmentation of the gingiva to improve smile esthetics and patient quality of life [1]. Most operative methods, including scalpel, abrasion, laser, and cryosurgery, leave an open wound that heals by secondary intention and may be associated with postoperative discomfort, delayed re-epithelialization, and suboptimal early healing [2,3]. Hyaluronic acid (HA) is a naturally occurring glycosaminoglycan of connective tissues and extracellular matrices. Its anti-inflammatory, anti-edematous, angiogenic, and cell-migration regulatory properties provide a biologic rationale for its use in operative wound care [5,6]. Clinical studies of HA in oral and periodontal surgery have reported improved epithelial closure, tissue color match, and postoperative comfort at donor and recipient sites, including free gingival graft and gingivectomy procedures [7-9]. Systematic reviews similarly suggest improved early wound-healing and patient-reported outcomes, although study quality, HA concentration, application protocols, and procedure types vary [6]. Post-surgical gingival repigmentation has also been documented after depigmentation procedures [4]. Evidence specifically addressing HA gel as an adjunct to gingival depigmentation remains limited. The study hypothesis was that topical HA gel applied after surgical gingival depigmentation would improve early wound healing and reduce postoperative pain compared with depigmentation without adjunctive HA. The null hypothesis was that there would be no statistically significant difference in early wound-healing outcomes or postoperative pain between groups.

Methodology

Study design and population

This prospective experimental clinical investigation assessed topical HA gel as an adjunct to surgical gingival depigmentation. The study followed the Declaration of Helsinki, received institutional and periodontal-department clearance at Attahadi University, and all participants provided written informed consent [16]. Systemically healthy patients with physiological maxillary or mandibular gingival hyperpigmentation were recruited from the Department of Periodontology outpatient clinic.

Eligibility criteria

Inclusion criteria were age 18-40 years, bilateral gingival hyperpigmentation requiring depigmentation, good oral hygiene (Plaque Index ≤ 1), and absence of periodontal disease. Exclusion criteria were conditions impairing wound healing, pregnancy or breastfeeding, allergy to HA, and antibiotic or anti-inflammatory medication use during the preceding three months.

Surgical procedure and HA application

Following phase I periodontal therapy, local anaesthesia was achieved using 2% lidocaine with epinephrine (1:100,000). Gingival depigmentation was performed by scalpel scraping or rotary bur abrasion until a smooth bleeding surface was obtained, followed by sterile saline irrigation and gentle pressure [1,3]. In the HA group, 1% HA gel was applied immediately after surgery; patients were instructed to reapply it with a clean fingertip twice daily for seven days and avoid eating or drinking for at least 30 minutes after application. Control patients received no topical HA.

Postoperative care and assessment

All patients were instructed to use paracetamol 500 mg as needed, avoid brushing the operated area for one week, and use 0.12% chlorhexidine mouthwash twice daily for seven days. No periodontal dressing was used. Early wound healing was assessed with the Early Wound Healing Index (EHI), where lower scores indicate better healing [17]. Complete epithelialisation was defined clinically as complete visual coverage of the treated wound by a continuous epithelial surface, with no visible open wound margins, no bleeding on gentle inspection, and no visible slough or raw granulation tissue; histological confirmation was not performed. Postoperative pain was recorded on a 0-10 visual analogue scale (VAS) on days 1, 3 and 7.

Clinical Cases

Gingival depigmentation cases with HA application were documented using standardised before, during, and after photographs to demonstrate procedural technique, healing progression, and esthetic outcomes.



Before



During



After

Figure 1. Gingival depigmentation: (A) before treatment, (B) intra-operative wound immediately after depigmentation, and (C) postoperative healing.

Statistical analysis

Statistical analyses were conducted using IBM SPSS Statistics for Windows, Version 26.0, with a two-tailed significance level of $\alpha=0.05$. Normality was assessed using the Shapiro-Wilk test. Independent t-tests and Mann-Whitney U tests were used for continuous variables, and chi-square or Fisher's exact tests for categorical variables. Repeated DOPI measurements were analysed with mixed repeated-measures ANOVA with Bonferroni correction. Kaplan-Meier analysis with the log-rank test assessed time to complete epithelialisation. Effect sizes and 95% confidence intervals were reported for major outcomes; post-hoc power exceeded 99% for the primary outcomes.

Results

Fifty patients were allocated equally to the HA group (n=25) and non-HA control group (n=25). Baseline demographic characteristics, Fitzpatrick skin type, pigmentation severity, and smoking status were comparable between groups.

Table 1. Baseline demographic and clinical characteristics

Parameter	HA Group (n=25)	Non-HA Group (n=25)	p-value
Mean age (years $\pm$ SD)	34.2 $\pm$ 8.5	35.1 $\pm$ 9.2	0.721
Sex (female/male)	18/7 (72%/28%)	17/8 (68%/32%)	0.754
Fitzpatrick skin type (III/IV/V)	5/12/8	4/13/8	0.892
Baseline DOPI score (mean $\pm$ SD)	2.84 $\pm$ 0.37	2.76 $\pm$ 0.44	0.492
Current smokers	4 (16%)	5 (20%)	0.715

DOPI = Dummett-Gupta Oral Pigmentation Index (0=no pigmentation; 3=severe pigmentation).

Anatomical distribution and surgical techniques

Treatment involved both arches in 96% of HA cases and 92% of controls; the remaining cases involved the upper posterior segment plus the lower arch. Bur abrasion was used in 72% of HA cases and 68% of controls, while scalpel excision was used in 28% and 32%, respectively. Neither distribution differed significantly between groups.

Table 2. Surgical techniques by group

Technique	HA Group (n=25)	Non-HA Group (n=25)	p-value
Bur abrasion (rotary instrument)	18 (72.0%)	17 (68.0%)	0.758
Scalpel excision (surgical blade)	7 (28.0%)	8 (32.0%)	0.758

Primary outcome: pigmentation reduction

DOPI scores were assessed at baseline, day 3, and day 7 by two independent calibrated evaluators; inter-rater reliability was high ($\kappa=0.89$). Baseline scores were similar. Importantly, the percentage values reported here do not represent the percentage of pigmented epithelium physically removed during surgery. Surgical depigmentation was performed to a clinically bleeding surface at the operative visit; therefore, the day-3 and day-7 measurements represent the postoperative clinical pigmentation score relative to each patient's baseline DOPI score. Percentage pigmentation reduction was calculated as $[(\text{baseline DOPI} - \text{follow-up DOPI}) / \text{baseline DOPI}] \times 100$. Thus, the observed difference reflects the extent of clinically visible residual/recurrent pigmentation during early healing, rather than incomplete surgical excision at the time of the procedure. By day 3, mean DOPI was 1.12 ± 0.33 in the HA group versus 1.68 ± 0.48 in controls. By day 7, mean DOPI was 0.08 ± 0.28 versus 0.64 ± 0.49 , corresponding to reductions of 97.2% and 76.8%, respectively. Between-group differences at days 3 and 7 were statistically significant ($p < 0.001$).

Table 3. Mean pigmentation scores (DOPI) over time

Time point	HA Group (n=25)	Non-HA Group (n=25)	Mean difference	95% CI	p-value
Baseline	2.84 ± 0.37	2.76 ± 0.44	0.08	-0.15 to 0.31	0.492
Day 3	1.12 ± 0.33	1.68 ± 0.48	-0.56	-0.79 to -0.33	<0.001
Day 7	0.08 ± 0.28	0.64 ± 0.49	-0.56	-0.78 to -0.34	<0.001

Complete pigmentation resolution (DOPI=0) by day 7 occurred in 92% (23/25) of HA patients and 48% (12/25) of controls, a 44% absolute difference (95% CI 22.7%-65.3%; $p < 0.001$). The reported odds ratio for complete resolution with HA was 12.42 (95% CI 2.56-60.31).

Secondary outcomes: healing and postoperative morbidity

Complete epithelialisation was defined clinically as complete visual coverage of the treated wound by a continuous epithelial surface, with no clinically visible open wound margins, no bleeding on gentle inspection, and no visible slough or raw granulation tissue. Histological confirmation was not performed. Using this clinical definition, mean time to complete epithelialisation was 5.9 ± 1.0 days in the HA group and 8.4 ± 1.6 days in controls, a 2.5-day reduction (95% CI -3.2 to -1.8; $p < 0.001$). Median times were 6.0 days (IQR 5.0-7.0) and 8.0 days (IQR 7.0-9.5), respectively. Kaplan-Meier analysis showed a significantly faster healing trajectory with HA (log-rank $\chi^2=18.34$, $p < 0.001$).

Table 4. Time to complete epithelialisation

Parameter	HA Group (n=25)	Non-HA Group (n=25)	Difference	p-value
Mean days $\pm$ SD	5.9 ± 1.0	8.4 ± 1.6	-2.5	<0.001
Median days (IQR)	6.0 (5.0-7.0)	8.0 (7.0-9.5)	-2.0	<0.001
Range (days)	4-8	6-12	-	-

Erythema was lower with HA on day 3 (1.08 ± 0.40 vs 1.96 ± 0.54 ; $p < 0.001$) and day 7 (0.12 ± 0.33 vs 0.56 ± 0.51 ; $p < 0.001$). Oedema on day 3 occurred in 8% of HA patients versus 32% of controls ($p=0.035$). Pain scores were lower in the HA group on day 3 (2.1 ± 0.9 vs 3.8 ± 1.2 ; $p < 0.001$) and day 7 (0.3 ± 0.5 vs 1.2 ± 0.8 ; $p < 0.001$). Mean satisfaction was higher with HA (4.7 ± 0.5 vs 3.9 ± 0.8 ; $p < 0.001$), with 96% versus 68% reporting satisfaction. No adverse events were reported in the HA group, compared with a 20% complication rate in controls ($p=0.025$).

Discussion

Topical HA gel used after surgical gingival depigmentation was associated with improved early healing, lower postoperative pain, and greater reduction in clinically assessed postoperative pigmentation scores. The findings are biologically consistent with HA's established roles in modulation of inflammation, angiogenesis, cell migration, and epithelial repair. The pigmentation findings should be interpreted as differences in postoperative clinical DOPI scores rather than differences in the amount of epithelium physically removed during surgery.

Clinical documentation of HA-treated cases indicated faster epithelial closure, smoother tissue surfaces, and reduced erythema during the first postoperative week, while untreated cases more often showed delayed epithelialisation, sustained inflammation, and greater discomfort. The findings are broadly consistent with previous studies of HA in oral wound healing. Yıldırım et al. reported enhanced epithelial closure and reduced burning at palatal donor sites treated with HA [7]; Özcan et al. reported reduced postoperative discomfort and improved palatal wound healing [8]; and Ustaoglu et al. found improved healing indices following gingivectomy with HA gel [9].

A systematic review by Rodríguez-Aranda et al. similarly highlighted potential angiogenic and anti-inflammatory benefits while noting heterogeneity in HA concentrations and application protocols [6]. This study adds preliminary evidence specific to gingival depigmentation, where secondary-intention healing and patient comfort are important. Although objective healing indices consistently favoured HA, subjective pain scores may vary with individual pain tolerance, oral ecology and surgical technique. The study text also notes that variation between scalpel and bur abrasion could influence tissue trauma, although subgroup analysis reported no significant technique-dependent differences in outcomes. Future studies should standardise operative protocols, HA concentration, and application frequency.

Limitations

The study had a relatively small sample size and short follow-up, limiting generalisability and preventing assessment of long-term tissue stability or repigmentation. Pain was measured with a subjective VAS, complete epithelialisation was determined clinically rather than histologically, and variation in surgical technique may have contributed to healing variability. The study did not compare different HA concentrations or application frequencies. Larger randomised controlled trials with standardised healing assessments and longer follow-up are needed.

Conclusion

In this comparative study of 50 patients, topical HA following gingival depigmentation was associated with greater reduction in clinically assessed postoperative pigmentation scores, faster clinically defined epithelialisation, less erythema and oedema, lower pain scores, higher patient satisfaction and fewer postoperative complications than depigmentation without HA. By day 7, the reduction in clinically assessed DOPI from baseline reached 97.2% with HA versus 76.8% in controls, and complete resolution (DOPI=0) occurred in 92% versus 48%. Mean epithelialisation time was 2.5 days shorter with HA (5.9 ± 1.0 vs 8.4 ± 1.6 days; $p < 0.001$). These results support further evaluation of HA as an adjunct in periodontal wound management.

Conflict of interest. Nil

References

1. Pogrel MA, Miller CE. A clinical study of gingival depigmentation. *J Oral Maxillofac Surg.* 2003;61(4):442-447.
2. Atsawasuwana P, Greethong K, Nimmanon V. Treatment of gingival hyperpigmentation for esthetic purposes by Nd:YAG laser: report of four cases. *J Periodontol.* 2000;71(2):315-321.
3. Murthy MB, Kaur J, Das R. Treatment of gingival hyperpigmentation with rotary abrasive technique. *J Indian Soc Periodontol.* 2012;16(3):417-421.
4. Dummett CO, Bolden TE. Post-surgical clinical repigmentation of the gingivae. *Oral Surg Oral Med Oral Pathol.* 1963;16(3):353-365.
5. Gupta S, Kumar A. Hyaluronic acid: molecular mechanisms and therapeutic trajectory. *Front Bioeng Biotechnol.* 2019;7:192.
6. Rodríguez-Aranda J, et al. Effect of hyaluronic acid on palatal wound healing: a systematic review. *J Oral Rehabil.* 2024.
7. Yıldırım G, Tözüm TF, Toy E, et al. Effect of topically applied hyaluronic acid on palatal epithelial wound healing: a randomized clinical trial. *J Periodontol.* 2018;89(3):283-292.
8. Özcan M, Ustaoglu G, Şen C. Effect of hyaluronic acid mucoadhesive on palatal wound healing and postoperative discomfort: a randomized clinical trial. *J Periodontol.* 2024.
9. Ustaoglu G, Şen C, Atagün ÖS. Efficacy of hyaluronic acid gel and photobiomodulation therapy on wound healing after surgical gingivectomy: a randomized controlled clinical trial. *BMC Oral Health.* 2023;23:519.
10. Bakhshi M, Rahmani S, Rahmani A. Lasers in esthetic treatment of gingival melanin hyperpigmentation: a review article. *Lasers Med Sci.* 2015;30:2195-2203.
11. Patel KA, Patil SS, Agrawal C, et al. Gingival depigmentation: case series. *Int J Appl Dent Sci.* 2015;1:37-39.
12. Ishikawa I, Aoki A, Takasaki AA. Potential applications of erbium:YAG laser in periodontics. *J Periodontal Res.* 2004;39:275-285.

13. Rosa DS, Aranha AC, Eduardo C de P, et al. Esthetic treatment of gingival melanin hyperpigmentation with Er:YAG laser: short-term clinical observations and patient follow-up. *J Periodontol.* 2007;78:2018-2025.
14. Lin YH, Tu YK, Lu CT, et al. Systematic review of treatment modalities for gingival depigmentation: a random-effects Poisson regression analysis. *J Esthet Restor Dent.* 2014;26:162-178.
15. Roshna T, Nandakumar K. Anterior esthetic gingival depigmentation and crown lengthening: report of a case. *J Contemp Dent Pract.* 2005;6(3):139-147.
16. World Medical Association. Declaration of Helsinki: ethical principles for medical research involving human subjects.
17. [Mounting artificial teeth]. PubMed. 1969.
18. Bertl K, Ebner M, Knibbe M, et al. How old is old for implant therapy in terms of early implant losses? *J Clin Periodontol.* 2019;46(12):1282-1293.
19. Pilloni A, et al. Early Wound Healing Index (EHI): a new index to evaluate early healing after periodontal surgery. *Clin Oral Investig.*
20. Hulbert WC, Duckett JW. Current views on posterior urethral valves. *Pediatr Ann.* 1988;17(1):31-36.