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ORIGINAL ARTICLE

Local application of hyaluronic acid in conjunction with free gingival graft: a randomized clinical trial

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Abstract

Objectives To assess the effect of the application of hyaluronic acid (HA) in conjunction with free gingival graft (FGG) on postoperative patient discomfort and wound healing.

Materials and methods A total of 24 healthy non-smoker patients requiring FGG were recruited for the study. Subjects were randomly assigned into study groups, local application of HA on both donor and recipient sites and control group, application of normal saline. The FGG dimensions were evaluated using digital photographs. Post-operative pain was evaluated for 14 days. Color matching and patient satisfaction were evaluated at 6 months.

Results In this randomized clinical trial, 21 patients (mean age 23 years, (15 females and 6 males) completed the study. Baseline characteristics were comparable across treatment groups. Pain scores in donor sites were statistically significant and higher in control group than study group until day 7 ($p < 0.05$). Mean of the surface area of the graft at baseline in study vs control group were (169 ± 21), (183 ± 22) (2 mm), respectively. While at 6 months, were (147 ± 30) and (139 ± 32) (2 mm), in study and control group, respectively ($p > 0.05$). Color match showed no statistical significance difference.

Conclusions Topical application of HA may exhibit significant improvement of postoperative pain and no significant difference in graft dimensions and patients' satisfaction.

Clinical relevance Topical application of HA is recommended as a dressing material in FGG surgeries to reduce postoperative pain and accelerate healing.

Keywords Gingiva · Graft · Tissue · Healing

Introduction

Free gingival graft (FGG) has been widely used to increase the width of attached gingiva [1]. Its autogenous character, maintenance of keratinization, ease of technique and high predictability of surgical outcomes altogether with the possibility of grafting in a group of teeth make the FGG to be accepted as the golden standard to increase the width of attached gingiva [2]. The main complication of FGG procedure is graft shrinkage post-surgically [3, 4]. Each time the FGG harvested from the palate that heals by secondary intention, patient suffered from postoperative pain and delayed healing [5]. Many hemostatic agents [6], dressing materials [7], and analgesics [8] have been used to reduce postsurgical pain.

To date, there is no definitive adjunctive material that can solve the problems associated with free gingival graft such as postoperative graft shrinkage, pain in both donor and recipient site, color mismatch between the graft and adjacent gingival tissue. Hyaluronic acid (HA) is a naturally occurring linear polysaccharide of the extracellular matrix of connective tissue, synovial fluid, and other tissues. HA has recently been introduced in reconstructive periodontal soft tissue surgery due to its significant structural, rheological, physiological, and biological functions with distinctive moisturizing, retention ability and viscoelasticity, coupled with its lack of immunogenicity and toxicity [9] which favor periodontal wound healing and regeneration. HA was recently suggested to be used as dressing material on the palatal donor site in FGG surgeries to reduce the post-operative pain and accelerate healing [10]. Previous in vitro and animal studies found

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that HA significantly increases the tensile strength of granulation tissue [11], stimulates clot formation [12], induces angiogenesis [13], and increases osteogenesis. A systematic review found that the topical application of HA could lead to faster healing after implant placement and sinus grafting procedures, leading to a reduction in patients discomfort [14]. A recent randomized controlled clinical trial showed that the use of HA in conjunction with autogenous soft tissue grafts may lead to excellent root coverage of single and multiple recession gingival recessions, which histologically may be accompanied by periodontal regeneration [15].

Specific objectives

The primary purpose of this randomized controlled clinical was to assess potential effect of the topical application of HA in conjunction with free gingival graft on postoperative pain at palatal donor site. The secondary outcomes were to assess the dimensional change and color match of the FGG.

Materials and methods

Study design and any changes after trial commencement

This single-center study was a 2-arm parallel randomized clinical trial with a 1:1 allocation. The methods were not changed after initiation of the trial.

Participants, eligibility criteria, and settings

An ethical approval for the conduction of this study was obtained from the Institution of Research Board Committee (IRB) at King Abdullah University Hospital/Jordan University of Science and Technology (JUST) in Irbid, Jordan and Jordanian Food and Drug Administration (Number: 29/135/2019). The study was performed in accordance with the International Conference on Harmonization Good Clinical Practice and CONSORT guidelines. The trial was prospectively registered with the clinicalTrials.gov (NCT04355325).

This clinical trial included 24 (17 females and 7 males) patients selected from patients scheduled for FGG treatment at the postgraduate clinics/Periodontics at JUST between July 2019 and January 2020. The study included patients who agreed to participate in the study and fulfilled the following inclusion criteria: Caucasian non-smoking patients aged between 18 and 50 years, presence of one or more sites (tooth) with inadequate width of KG labially < 2 mm (in the anterior area (canine to canine) of the lower jaw, absence of pericoronitis or signs of inflammation during the last 30 days, no active diseases, and good oral hygiene. Exclusion criteria were: female subject who was pregnant or lactating, patients who participated in any clinical research study within the previous 8 weeks and patients on anti-coagulant drugs and those with abnormality of wound healing process.

Participants of the study were selected based on the inclusion and exclusion criteria. After explaining the study and its implications, informed consent was signed by the patient.

Interventions

For all patients included in the study, phase I periodontal therapy was completed 4 weeks pre-surgically. All data registration and surgical procedures were done by a specialized periodontist (SK). Prior to the surgery, all patients were instructed to gargle with anti-microbial chlorohexidine mouthwash (0.2%) for one minute to help in the reduction of bacterial load in the mouth due to the bactericidal effect of this mouthwash. Local anesthesia (by 2% lidocaine with 1:100 000 epinephrine) was given into the depth of the vestibule at the recipient site and at donor site.

On the recipient site, two teeth were treated in the area (canine–canine) coronal incision was made horizontally at the level of mucogingival junction on the teeth to be treated and passing the midpoint of the adjacent teeth, at right angle 90° to the mesio-angle and disto-angle to the papilla to create "Butt joint" margin. The recipient sites had even thickness of the flap, then the flap was repositioned apically.

On the palatal donor site, custom tinfoil template was placed over the palatal mucosa to outline the dimensions of the graft according to the recipient bed. The outlined graft was harvested carefully as follows. The surgical blade (1/4 length of knife edge of the blade that approximately 1.4–1.6 mm in depth) was entered in the contour incision.

The area chosen to harvest the graft was between first premolar and first molar and located 2 mm distant from the gingival margins of the corresponding teeth carefully as follows. After harvesting the FGG, raft thickness was immediately confirmed with a digital caliber at 5 points (four corners and center of the graft) and, if necessary, the graft was prepared (thinned) while holding it on sterile tongue depressor to obtain a graft approximately 1 to 1.3 mm thick. Then, the graft kept on sterile gauze soaked with normal saline until graft stabilization.

Photograph was taken immediately to measure the graft area at the baseline. Connective tissue surface was carefully inspected for irregularities or adipose tissue after graft separation to minimize dead space between the graft and the recipient bed and enable quick revascularization of the FGG. Graft thickness was immediately confirmed with a digital caliber at 5 points (four corners and center of the graft). Depth of the blade incision was standardized to guarantee equal depth in all samples.

In the study group (SG), HA (HYADENT BG)™ was applied topically to the entire recipient bed prior to graft placement in the prepared bed, after the bleeding stopped. HA was applied only once. In the SG, (HYADENT BG)™ was applied on the donor site as well and injected in the collagen sponge that was placed over the donor site. In the control group (CG), HA was neither applied to the recipient nor the donor sites. In the CG; the recipient site was washed with normal saline before the graft placement and the donor site was washed with normal saline and placing the collagen sponge that soaked in normal Saline on the donor site.

For both groups, the donor sites, a collagen sponge, and figure X -0 resorbable sutures were placed. Finally, covering the donor areas in both groups with Septo-pack gingival dressing\

(Septodont, Saint Maur-des-fosses, France) then X suture over the pack to prevent the displacement of pack (Fig. 1). At the recipient site, minimal and fixed number of sutures were used for stabilization of the FGG as described previously by (Sullivan, 1968). Suturing the graft was done under magnification using Dental magnification loupe (3.5X-420 mm). The Graft was stabilized in both groups using (6–0 polyglycolic acid/ reverse cutting/12 mm suture) with two simple interrupted sutures in the coronal portion of the two Apico-coronal edges, and one suture in the mid-point of the coronal border using simple interrupted method. One Periosteal Oschenbein suture (4–0 polyglycolic acid/ reverse cutting/12 mm suture) was used to fix the graft on its place.

In the SG, the operator topically applied the HYADENT BG™ on the borders of the graft after before stabilization of the graft as placebo. Finally, after stabilization, gentle direct pressure to the graft for five minutes in both groups to stabilize the clot under the graft. The surgical procedures were conducted by the same periodontist (SK).

Postoperative instructions were given to both groups and include ceasing tooth brushing or flossing around the surgical sites until the day of periodontal sutures removal (day 14). However, patients were directed to start brushing their teeth expect the experimental area (canine to canine) after one week and to eat only soft foods during the first week and to avoid any mechanical or thermal trauma. Patients were followed-up by the same periodontist (S.K.), and scheduled to be seen at 1 month, 3 months and 6 months after the surgery.

Outcomes (primary and secondary) and any changes after trial commencement

Primary outcomes

Visual analogue scale (VAS) was used to evaluate the pain for two weeks after surgery. A two separates 10 cm VAS with 'no pain' at the left and 'unbearable pain' at the right end as verbal end points. Two forms for each day, one for the recipient site and one for the donor site. Forms were given to subjects after completion of the FGG surgery and they asked to mark the pain value they feel at the end of each day. Forms were collected on the day of suture removal (day 14).

Secondary outcomes

Clinical photographs were used to measure the surface area of the graft at day of surgery and at follow-up visits and to assess the color matching between the grafted area and the adjacent tissue at the 6-month visit. All intra-oral photographs were taken with the same professional camera (Nikon D3400) with the same intraoral photographs setting (Aperture 32, Shutter speed 1/160, ISO 100), professional macro lens (Sigma 105 mm f/2.8 EX DG OS HSM Macro Lens), ring flash (Godox Macro Ring Flash ML-150) with ½ light exposure. Fixed distance between the chin of the patient and the ring flash was considered to take that the photograph was 30 cm. Lip retractor was used to allow uniform lighting of the area, and using Michigan "O" periodontal probe parallel with adjacent teeth as a reference (known distance between two fixed points) for measuring the graft area using the digital software.

The graft area measurement was performed with Java-based analyses program (ImageJ, National Institutes of Health, Bethesda, MD, USA) (Fig. 2). Digital evaluation to measure the shrinkage was proffered comparing to clinical evaluation because the grafted tissue shrinks in uneven

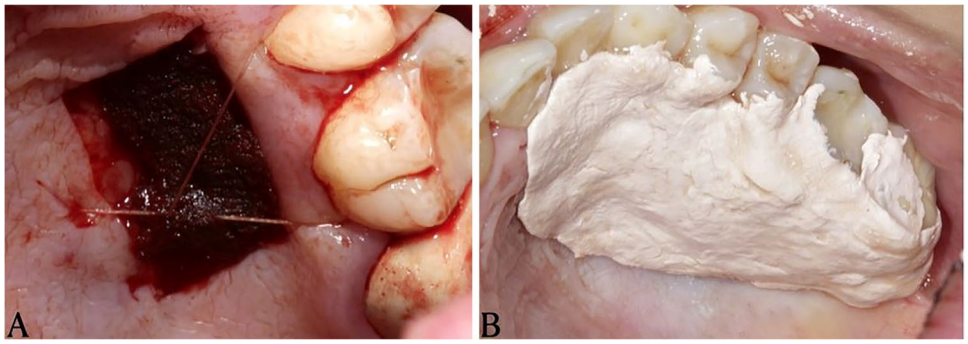

Fig. 1 **A** Donor site management with collagen sponge injected with HA (HYADENT BG), and stabilization of sponge with figure X suture. **B** Complete closure of the donor site

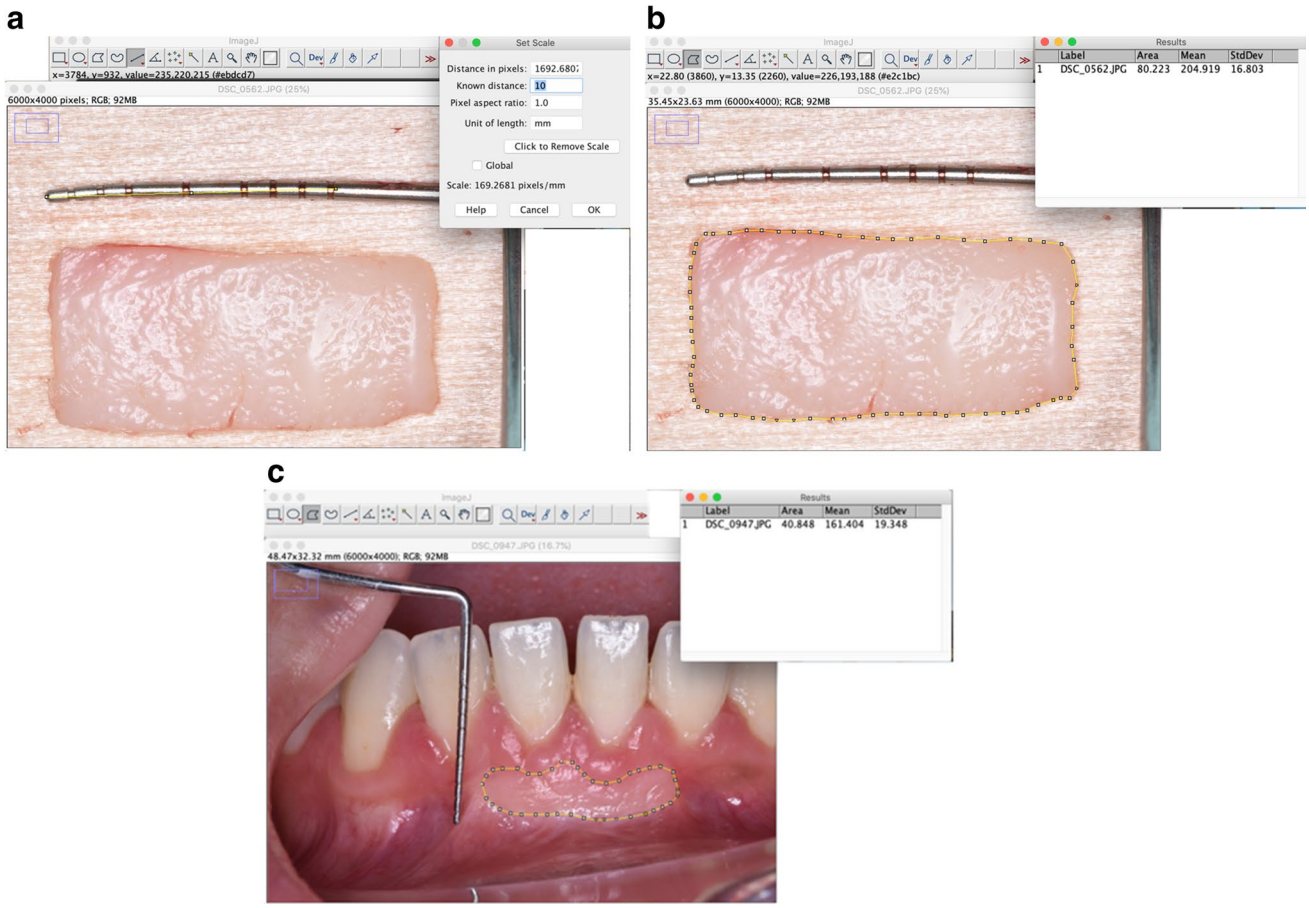

Fig. 2 **A** Illustration of measuring the distance between two fixed points calibrated by pixel numbers. **B** Illustration of analyzing the surface area of the graft at baseline after harvesting. **C** Illustration of analyzing the surface area of the graft in follow up visits

way. Moreover, measuring the surface area using just periodontal probe was not highly sensitive. For evaluation of the graft area, graft borders were drawn after inserting the known distance between two fixed points on periodontal probe (10 mm) by the number of pixels between these two points. All evaluations were repeated twice, and the average value of these two measurements was calculated at 1-, 3-, and 6-month follow-up visits.

Patient's satisfaction was measured at 6 months post-surgically using a scale from 0 to 10 which was filled by each patient. On this scale, 0 is not satisfied, little satisfied (1–3), average satisfied (4–6) and highly satisfied (7–10) is fully satisfied by the outcome.

Sample size calculation

Power calculation was performed at $\alpha = 0.05$ and at $\beta = 0.20$, equal to 80% of power (by using Graph Pad Software, InStat‡) as reported by Yıldırım et al. 2018 [10]. Under this assumption, at least 10 patients were needed for each group. Twelve patients per group were included for any possible dropouts.

Interim analyses and stopping guidelines

Not applicable.

Randomization (random number generation, allocation concealment, implementation)

Participants were randomly allocated to either HA or normal saline groups. Randomization sequence was created using Excel 2010 (Microsoft, Redmond, WA, USA) with a 1:1 allocation using random block size 2. Allocation concealment was applied before the trial commencement to prevent selection bias. The allocation sequence was concealed in sequentially numbered, opaque, and sealed envelopes from the investigator responsible for assigning participants into the intervention groups (RA) until the time of allocation implementation. Randomization sequence creation and allocation concealment were applied by another operator (SA).

Blinding

Blinding of the investigator was not possible during the clinical intervention and only participants were blinded to the type of material used. Blinding of the investigator was implemented at data measurement stage as the investigator (SK) was blinded. The investigator (MA) who did the statistical analysis was blinded to the material used in each group.

Statistical analysis (primary and secondary outcomes, subgroup analyses)

Data analysis included descriptive and analytic statistics obtained with Statistical Package for the Social Sciences (SPSS) software, version 26.0 (Chicago, IL, USA). Data were checked for normality. Descriptive statistics were calculated and both study groups were compared for pretreatment characteristics. Comparisons were conducted using *t*-test or chi-square test, depending on the examined variable (numerical or categorical). Statistical significance was predetermined at the $P \leq 0.05$ level for all tests.

Chi square was performed to provide valuable statistical insight, as well as to see the differences between group characteristic of participants. Inferential analysis was utilized to meet the specified objectives. Mann–Whitney U evaluated the differences of pain score patient satisfaction and color match within and between SG and CG at baseline and after treatment. Two-way repeated measure ANOVA was used for comparisons in shrinkage differences between and within the groups. Wilcoxon test was used to determine the mean scores to evaluate the differences of pain score patient satisfaction and color much between SG and CG and between recipient site and donor site groups.

Measurement error

All measurements were performed by a single calibrated examiner (SK). A random sample of 4 patients photographs images were re-evaluated after 2-week interval. The interclass correlation coefficient was for the mean change in graft area found to be above 90%.

Results

Participant flow

CONSORT flow chart showing the flow of participant data through the trial is presented in Fig. 3. Twenty-four patients who required FGG for the lower anterior segment were recruited from July 2019 to January 2020 with final data collection completed in September 2020. The sample was randomized in a 1:1 ratio to either group. Three patients (13%) were excluded as they failed to attend the clinic at the recall visits. Complete data were collected for 21 patients (Study group, 11; control group, 10).

Baseline data

Subjects assigned to the study group consisted of 6 females and 5 males with a mean age of (32 ± 2) years and subject assigned for the control group consisted of 9 females and 1 male with (Mean age: 33 ± 1 years).

Primary outcomes

The level of pain score at the donor sites was significantly higher in the control group than study group in the first seven days (Table. 1) (Fig. 3). Comparing the level of pain in donor site over the time showed that there were significant changes over the time in both study ($Z = 134.039$, $p < 0.001$) and control group ($Z = 123.042$, $p < 0.001$) (Fig. 4).

The level of pain score at the recipient site was significantly higher in the control group than study group only at day 1 (Table 2). Comparing the level of pain in recipient site across the time, results indicated that there were significant changes over the time in both test ($Z = 122.601$, $p < 0.001$) and control group ($Z = 116.564$, $p < 0.001$) (Fig. 5).

Secondary outcomes

Color match of FGG for each patient in both groups were assessed by two blinded examiners. The average mean score of color match from both blinded examiners was 6.25 for study group and 6.77 for the control group with no statistically significant difference between both groups ($Z = 1.182$, $p = 0.251$).

Graft area showed that the main effect of the group (study and control) on graft area was not statistically significant ($F(1, 19) = 0.171$, $p = 6840.001$, $\eta 2 = 0.000$). Mean of the surface area of the graft at baseline in study vs control group were (169 ± 21) and (183 ± 22) (2 mm), respectively. While at 6 months were (147 ± 30) and (139 ± 32) (2 mm), in study and control group, respectively, with no statistically significant difference between groups ($P > 0.05$) (Table 3). The findings for within subjects' effect of repeated measures across the time for mean graft area was significant ($F(3, 57) = 6.049$. $p = 0.001$, $\eta 2 = 0.241$). These results indicated that the interaction between group and time for graft area shrinkage was not statistically significant ($F(3, 57) = 0.538$. $p = 658$, $\eta 2 = 0.028$) which means that groups had the same pattern over the time (Baseline, 1 month, 3 months, 6 months) for graft area. Comparing the mean graft area shrinkage between two groups across the time results revealed that

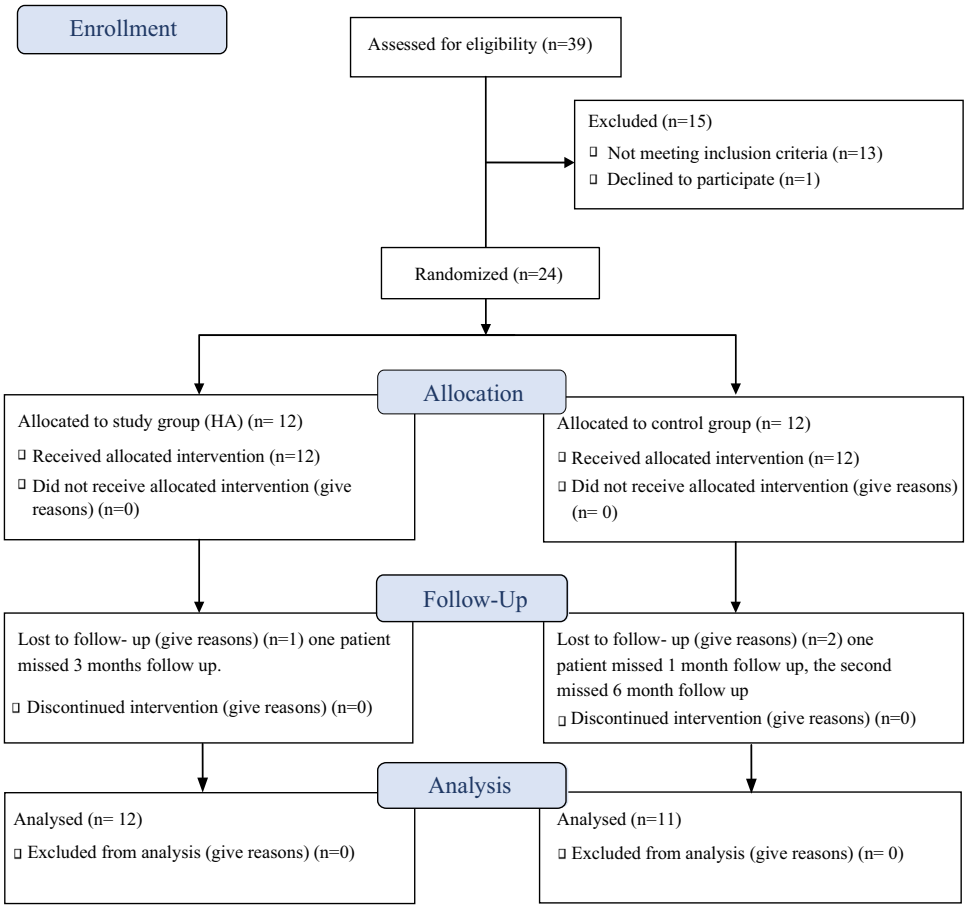

Fig. 3 CONSORT flow chart

Table 1 Comparison of median pain scores in donor site between groups

Day	Groups median (IQR)		Z value	*p* value
	Study	Control		
Day 1	5(1)	8(1)	− 3.957	< 0.001
Day 2	5(2)	8(2)	− 3.576	< 0.002
Day 3	3(2)	6(2)	− 3.644	< 0.003
Day 4	3(2)	4.5(2)	− 2.203	0.028
Day 5	2(2)	4(2)	− 2.535	0.011
Day 6	1(1)	2.5(3)	− 2.154	0.031
Day 7	1(0)	2(1)	− 1.997	0.046

the graft area shrinkage between study and control groups was always not statistically significant ($p > 0.05$) (Baseline, 1 month, 3 months, 6 months) (Table 4).

Total scores of patient's satisfactions showed that patient's satisfactions in study group (M = 8.82) and control group (M = 8.70) were not statistically different (t = 0.242, $p = 0.811$).

Harms

No negative outcomes were reported by any subject during the trial.

Discussion

Free gingival grafting is the first recommended approach for the treatment of inadequate keratinized gingiva. However, FGG is a technically demanding procedure and associated with pain and delayed healing [6]. To the best of our knowledge, this is the first reported randomized clinical trial that used HA in both donor and recipient sites to assess if it can be advantageous in FGG surgeries.

Postoperative pain was assessed directly by the patient using VAS scale for 14 days after surgery on both donor and recipient sites in both groups. No analgesics were prescribed. Previous studies [16, 17] evaluated the postoperative pain indirectly based on mean consumption of analgesics which is considered as a more quantitative method.

In our study, we used periodontal dressing for palatal wound care, wound protection, pain reduction as well as

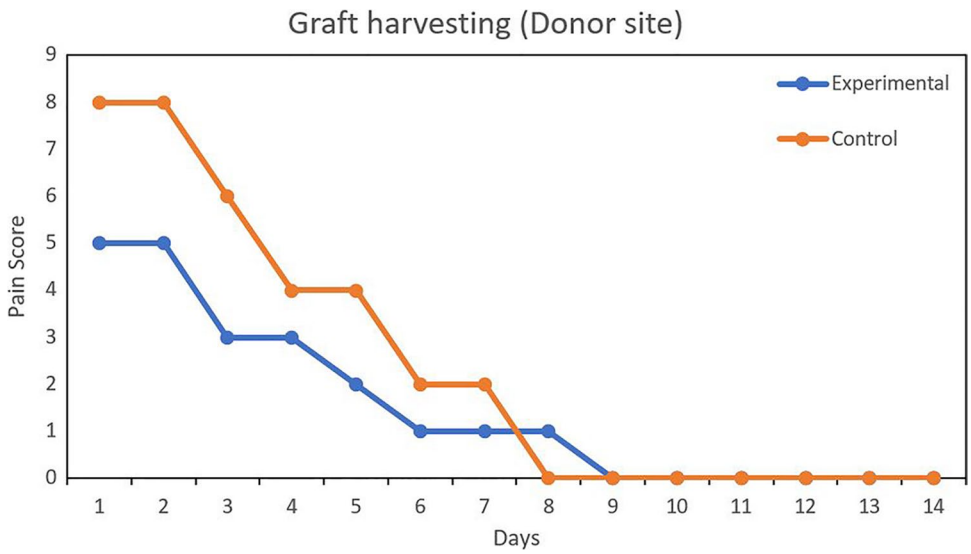

Fig. 4 The pain score in donor site for both groups for 14 days

Table 2 Comparison of median pain scores in donor site within groups

Day	Groups median (IQR)		Z value [a]	*p* value [a]
	Study	Control		
Day 1	4(2)	7(2)	− 2.648*	0.008
Day 2	3(2)	5(3)	− 1.682	0.093
Day 3	2(3)	3(3)	− 1.322	0.186
Day 4	2(2)	3(2)	− 1.444	0.149
Day 5	2(2)	2.5(2)	− 1.228	0.22
Day 6	1(1)	1.5(1)	− 1.079	0.281
Day 7	0(1)	1(2)	− 1.274	0.203

HA retention [18]. The periodontal dressings were applied to the donor sites in both groups and were kept in place at least for the first week. We did not renew the dressing and re-applying the HA to avoid traumatizing the wound and to prevent any infection of the wound during the exposure, and to mimic the daily practice settings where it is difficult for the patient to attend multiple visits in the first week post-surgery.

Our results came in agreement with Lee et al. study [19] who reported pain improvement in 76% of the patients in 2 weeks in which 0.2% HA gel was applied to recurrent aphthous ulcers and the oral ulcers of Behçet's disease patients. On the other hand, our results disagreed with Yıldırım et al.

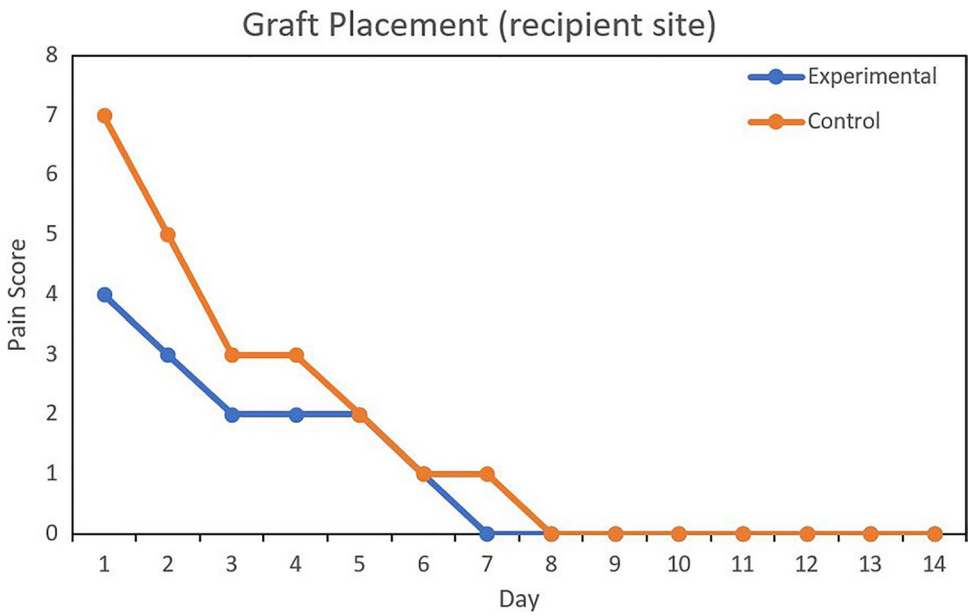

Fig. 5 The pain score in recipient site for both groups for 14 days

Table 3 Descriptive of statistics of graft area shrinkage

Time	(I) Group	(J) Group	Mean Difference (I-J)	SE	*p* value
Baseline	Study	Control	− 13.816	9.515	0.163
1 month	Study	Control	− 6.543	14.768	0.663
3 months	Study	Control	− 1.011	15.507	0.949
6 months	Study	Control	7.342	13.58	0.595

Table 4 Summary of RM-ANOVA for graft area

Time	(I) Group	(J) Group	Mean difference (I-J)	SE	*p* value
Baseline	Study	Control	− 13.816	9.515	0.163
1 month	Study	Control	− 6.543	14.768	0.663
3 months	Study	Control	− 1.011	15.507	0.949
6 months	Study	Control	7.342	13.58	0.595

study [10] who reported that pain score was significantly more in control group without periodontal dressing alone to the palatal wound compared to the 2 study groups (test-1 0.8% HA, test-2 0.2% HA). Tavelli et al. [20], used different materials to protect the palatal wound, and the lowest pain score in their study was with cyanoacrelate and hemostatic gelatin sponge group in the first two days post surgically.

Our results showed that HA has longer effect on donor site postoperative pain until day 7, and that may be explained that HA helps in angiogenesis and clot stabilization that accelerates the healing time of the donor site. This was in agreement with Keceli et al. [6] who reported that mean VAS pain scores were significantly higher in control group at the first six postoperative days. However, comparing HA with *Alpinia officinarum*, the *Alpinia officinarum* material might play a role as a scaffold for the bacteria because it lacks the antimicrobial effect and therefore, might increase the risk of donor site infection. Our results disagreed with a study conducted by Sousa et al. [21], who compared palatal wound healing and pain using A-PRF clot membrane as test group, and gelatin sponge as control group. They reported that pain was significantly less in the test group in the first two days only [21]. However, in their investigation, the thickness of the graft was not measured, which may explain the powerlessness with postsurgical pain that occurred in the donor site. Moreover, they did not cover the donor site with periodontal dressing neither palatal stent that may have explained that the effect of A-PRF on pain was only on the first two days post-surgically. Comparing HA with platelet concentrate (PC) in covering the donor site, PC did not influence complication occurrences or mediate pain level [22]. HA helped in reducing pain in recipient sites only if the first day post-surgically, and this may be explained by the recipient site was not covered and the HA was not retentive under the FGG. Therefore, the HA in the recipient site was washed out by saliva and gargling with mouth wash after day 1.

A previous study reported a positive relationship between graft thickness and the patient's score of pain, but the present study's results did not confirm such a relationship [23]. This discrepancy might be attributed to the variations in graft thickness between both studies; Burkhardt et al. reported that grafts of more than 2 mm in thickness were associated with a higher morbidity [23], but in the present study, no graft was thicker than 1.3 mm.

Comparing our study to others who used PRF as dressing material to reduce palatal pain after CTG harvesting, PRF reduced postoperative pain at 3rd and 7th day, and analgesics taken were significantly lower in the same days mentioned above [24].

The FGG shrinkage showed that the main effect of the group on graft area shrinkage was not statistically significant. Our explanation of this result, that continuity of graft nutrition plays a major role in graft shrinkage. In addition, in the current study, the graft thickness was standardized (1–1.3 mm) in both groups, and size and number of sutures was also standardized. Our finding was in agreement with Sullivan [25] who reported that thickness of the graft, atraumatic surgical technique and quick stabilization of the graft are vital to prevent damaging of the graft vessels and dehydration, thereby decreasing shrinkage [25]. Also, suture technique is also highly important for minimizing trauma to the graft tissue. Therefore, it is recommended to keep the number of sutures to a minimum since each suture formed a localized hematoma under the graft which affect graft shrinkage. Moreover, the non-significant difference of graft shrinkage between both groups indicated that the stabilization method of FGG mainly affected the shrinkage of the graft. This was in agreement with Gümüş and Buduneli [26] who used different stabilization method by cyanoacrylate and sutures, and reported that in cyanoacrylate group, the graft shrinkage was significantly less than stabilizing with sutures. No published study with similar study groups could be found to compare with our results. We believed that surface area digital calculation by software enabled more sensitive assessments because of irregular patterned of graft shrinkage. At the end of the present study, all subjects in both groups having at least 3 mm of keratinized tissue width in the treated sites. The color match between grafted area and adjacent keratinized tissue was not affected by HA used, and that was explained by, since the graft comes from the palate which contain of lipid contents, color difference is so obvious that the grafted area looks lighter in color even in a long time after initial healing [27]. Moreover, the specificity of the grafted epithelium is determined by the underlying connective tissue, and the gingival connective tissue is

able to generate the keratinized epithelium [28]. Patient's satisfaction was not affected also and that was explained by that HA has no effect on color match also. We believed that the use of HA especially in the donor palatal site that most of the patient refused the treatment because of the unbearable pain occurred in donor site post surgically, may help the patients accepting the idea of having palatal donor site in daily practice in the clinic and decrease the postsurgical morbidity in the palatal wound.

Limitations

1. In our study, most of the patients were females who are more likely to seek for dental care and correction of mucogingival defect. However, this might affect the generalization of our results to all patients.
2. Factors that might affect interpretation and comparison of results are patient compliance, using professional evaluation of the color match which was subjective rather than using objective measures such as digital evaluation of the color match. Moreover, difference of graft size at baseline depending on the mucogingival defect in each site treated.
3. Our resuklts was not confirmed with histology to evaluate true healing. However we believe that clinical asssessment reflectsearly healing, that dictate the outcomes of wound healing

Conclusions

Despite the limitations of this study, the results suggest that HA accelerates the healing process by promoting an apparent less painful postoperative period. Larger sample size is recommended with a longer follow-up period and using a split mouth technique in future studies by comparing the effect of hyaluronic acid with other treatment modalities.

Funding This study was supported by the Deanship of Research/Jordan University of Science and Technology.

Data availability The datasets generated during and/or analyzed during the current study are available upon request.

Declarations

Ethics approval and consent to participate The study was independently reviewed and approved by the Institutional Research Board of Jordan University of Science and Technology. Written consent was obtained before interview and after explaining the study purposes, methodology and possible future publication of clinical datasets according to the Declaration of Helsinki.

Informed consent Informed consent was obtained from all individual participants included in the study.

Conflict of interest Sooud Khalil declares that he has no conflict of interest. Rola Al Habashneh declares that he has no conflict of interest. Sawsan Alomari declares that he has no conflict of interest. Majdi Alzoubi declares that he has no conflict of interest.

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