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Effect of honey dressing material on palatal wound healing after harvesting a free gingival graft: a prospective randomized case control study

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Abstract. – OBJECTIVE: The aim of this prospective randomized case-control study was to understand the clinical benefits and effect of honey as a dressing material on palatal wound healing after harvesting free gingival graft (FGG).

PATIENTS AND METHODS: This prospective randomized case-control study was conducted on a sample of 20 patients with 10 patients in each group. Medihoney dressing material was applied to the donor site in the test group, whereas no dressing material was applied to the control group. All the patients received the same medication (Ibuprofen 600 mg) and post-operative instructions straight away after the surgical procedure. Patients were given the follow-up appointment at first, second and fourth week after the surgery during which the length and the width of the donor site was measured and recorded.

RESULTS: At first week, a significant difference in the proportion of patients showing the healing of donor site percentage was found to be 56% (both in width and length) for test group vs. 44% (both in width and length) for the control group (p=0.001). At 4-week, the healing of donor site percentage was found to be 86% (in width) and 91% (in length) for test group vs. 14% (in width) and 9% (in length) for the control group, the difference being statistically significant (p=0.001).

CONCLUSIONS: The result of this current study suggests that the honey dressing material accelerated the wound healing process of the palatal wound after harvesting FGG. It also showed a shorter recovery period along with less post-operative morbidity.

Key Words:
Cytokines, Donor, Morbidity, Neutrophils, Pain, Periodontist.

Abbreviations

FGG: Free Gingival Graft, FDA: Food and Drug Association, CI: Confidence Interval PRF: Platelet Rich Fibrin, SD: Standard Deviation, VAS: Visual Analogue Scale.

Introduction

The most suitable area for harvesting a free gingival graft (FGG) in periodontal surgery is hard palate. Palatal grafts exhibit exceptional clinical results because of their autogenous nature which makes them preferable over other allogenic or synthetic grafts[1]. It generally takes two to four weeks for the open wound to heal after harvesting the FGG from the donor site[2,3]. There are many phases in the wound healing process which makes it complex in nature. The initial phase is known as hemostatic phase where platelet cells start healing the wound by forming the blood clot. Other blood cells composed of vitronectin, fibrin and fibronectin also play the similar role simultaneously. The next stage is inflammatory phase where monocytes and neutrophils play a preliminary role in wound cleansing. Then, granulation tissue forms in the formation phase,

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which is later replaced by the provisional connective tissue. In this phase, endothelial, fibroblasts and epithelial cells are involved in capillary formation, connective tissue formation and re-epithelialization, respectively. Finally, in modelling phase, regeneration of the tissue takes place from the collagen-rich dense matrix. Pain, discomfort and bleeding are the most common side effects of FGG harvest in hard palate which may upset patients' quality of life including disturbance in speaking, eating and drinking. Hence, it is necessary to evaluate the quality of life of the patients who have undergone a soft tissue grafting in clinical trials[4-6]. Previous research compared the results of different retainers, such as modified Hawley retainer, Essix retainer, modified Essix retainer and periodontal dressing on patients' appearance, pain, chewing and speaking which showed that periodontal dressing caused bleeding and more pain after one week of surgery. Whereas visual analog scale (VAS) scored lower in appearance and speaking with periodontal dressing, on the other hand, retainers exhibited the opposite results than the periodontal dressing[7]. Another study[8] used platelet-rich fibrin (PRF) and hyaluronic-acid gels at the donor site after harvesting the FGG and found both PRF and hyaluronic-acid gel significantly decreased the pain and was advantageous for the wound healing parameter. A study[4] also assessed the efficacy of herbal extract, which was placed after harvesting FGG, following which minor pain was observed along with less primary and secondary bleeding after a week of surgery. In addition, a case control study[9] reported that ozonated oil significantly accelerated the wound epithelialization in palate in the treatment group in comparison to the control group.

Leptospermum species tree form Australia and New Zealand is a great source of honey and their preparations have been studied previously. These specific species of honey are well-known for the bactericidal properties and are widely distributed in the United States as 'medical-grade honeys' (MGHs) in numerous formulations and trade names. These MGHs are used as a dressing material and the honey contained in MGHs provide additional complementary media which helps in moisturization and removes the damaged tissue from the wound[10]. There are different types of honey available with comparable properties, such as Manuka honey and Medihoney; however, honey from different plants shows altered antibacterial properties. Most of the studies related to medicated honey were conducted on New Zealand based Manuka honey from Leptospermum species[11]. Since honey was being used as a medicament, many honey products are being launched with the approval of FDA. Moreover, many clinical studies including case-control, randomized clinical trial and cross-sectional studies are utilizing honey in distinctive types of wound healing in different medical specialties.

Honey has anti-bacterial properties which facilitate the wound healing and minimize the bioburden of the wound. It also has been reported to be effective against *S. Aureus*, *Pseudomonas aeruginosa*, *Stenotrophomonas*, *Acinetobacter* and *Escherichia coli*. One previous study[12] stated that manuka honey increases the cytokines and prostaglandin E_2 production from monocytes, the macrophage precursor cells. Macrophages have many functions in wound healing from removing the wound debris to new blood vessels formation. Moreover, another recent study revealed that honey has the radical scavenging activity which supports the finding of previous studies that honey acts as an antioxidant and protects the cell damage from the free radicals[13,14].

Although there are many benefits of honey in terms of wound healing, limited research has been conducted on the effects of honey on oral wound healing. Therefore, the aim of this prospective randomized case-control study was to understand the clinical benefits and effect of honey as a dressing material on palatal wound healing after harvesting FGG.

Patients and Methods

Study Design, Setting, Sampling, and Ethical Considerations

This prospective randomized case-control study was conducted on a sample of 20 patients with 10 patients in each group. The sample size was calculated where the power was 90%, type I error was 5% to reveal the difference in the percentage of patients that showed palatal wound healing after 4 weeks either who applied the honey dressing material (test group) or who did not receive any dressing material (control group).

The study was conducted between February 2020 and May 2020, and included patients referred to the periodontal clinics at Riyadh Elm University (Riyadh, Saudi Arabia). Twenty patients were chosen who needed to increase their keratinized tissue or to treat their gingival reces-

sion. For randomization, initial 10 patients were assigned for the test group and the following 10 patients were assigned to the control group.

This prospective randomized case-control study was approved by the Institutional Review Board (IRB) at Riyadh Elm University. The IRB approval number is FPGRP/2019/438/36/80 and the study was also registered in ClinicalTrials.gov (NCT04269694). Written informed consent was obtained from each subject. The participants were informed about the exact procedure of the study.

The inclusion criteria: patients participating in the study should be an adult (18 years or more), non-smoker, with no systemic disease and score of full-mouth plaque and bleeding less than 20%.

Exclusion Criteria

Patients participating in the study should not have any history of mucogingival surgery on the palate, pregnant patients, any medicine or systemic diseases that interfere the wound healing, patients on corticosteroids and patients with coagulation disorders.

Clinical Parameter and Procedures

An initial periodontal examination and treatment were provided to the patients if required prior to any other procedure. Full-mouth bleeding and plaque score of the participants were checked, if the results were <20%, then, they were included in the study. Same periodontist performed the surgical procedures and same periodontal probe (Hu-Friedy PCPUNC 15 mm, Hu-Friedy, Chicago,IL) was used to record all measurements. Local infiltration with 1.8 ml lidocaine 2% 1:1000000 epinephrine was used to achieve the anesthesia in the donor site on the palate. The width and the length of the donor site were measured and recorded. Medihoney dressing material (http://www.medihoney.com) was applied to the donor site in the test group. No dressing material was applied in the control group. Glucose oxide and Leptospermum are the two main components in the Medihoney that provide the bactericidal activity. Moreover, it is lawfully used in many countries for wound healing, such as USA, Australia and Europe. It aids the natural process of wound healing and stimulates the elimination of devitalized tissue. This Medihoney contains low pH (3.5-4.5) which assists to lower the pH level in the wound area and promotes wound healing[15].

All patients received the same post-operative instructions straight away after the surgical procedure. They were advised to take soft diet along with one tablet of Ibuprofen 600 mg at every eight hours along with chlorohexidine 0.12% mouth rinse to be used twice a day. Patients were asked to note down the level of pain and discomfort (speaking, eating, etc.) for one week after the surgery using the VAS graphic format where pain score was scaled from zero to ten. Irritating sensations, as well as difficulty in speaking, eating etc., were defined as discomfort and pain was described as inability to function needing painkiller medication. Patients were given the follow-up appointment at first, second and fourth week after the surgery during which the length and the width of the donor site was measured and recorded.

Statistical Analysis

Statistical analyses were performed in IBM SPSS Statistics 25 (IBM Corp., Armonk, NY, USA) software. Inferential statistical methodologies were applied. As for the descriptive statistics that were used, they were [mean, median, standard deviation (SD), range, and mode]. 95% confidence interval (CI) was used to estimate the population means. Spearman order correlation coefficient statistical test was performed to identify the level of post-operative pain and the level of discomfort from the donor site. Total length and width ratio between two groups was analyzed using the *t*-test. The p-value < 0.05 was considered as statistically significant.

Results

A total of 20 patients were participated in this prospective randomized case-control study. The mean age was 35 years, and the female/male ratio was 10/10. Table I and Figure 1 shows the mean (width and length) of the donor site measurements and standard deviation in the follow-up period.

Table II shows the results of the donor site measurements wound area can be presented in the follow-up period (four weeks). The difference can be seen between the test group of all honey dressings where the palate attaches and the control group.

At first week, a significant difference in the proportion of patients showed the healing of donor site percentage and we found it was 56% (both in width and length) for test group *vs.* 44% (both in width and length) for the control group (p=0.001). At 4-week, the healing of donor site percentage was found to be 86% (in width)

Table I. Donor site measurements (mm), presented as mean (standard deviation – SD) and estimated mean (95% CI), evaluated at surgery and along the follow-up visits, for the control. (n=10) and test (n=10) groups.

Follow-up weeks	Test Group		Control Group	
	Mean (W, L)	Std. Dev (W, L)	Mean (W, L)	Std. Dev (W, L)
0-Week (surgery)	6, 11.2	0, 1.03	6, 11.4	0, 1
1-Week	4.2, 8.2	0.63, 2.5	5.4, 10.4	0.7, 1.2
2-Week	2.5, 4.8	0.85, 2.2	4.4, 9.1	0.8, 1.2
4-week	0.4, 0.4	0.7, 0.7	2.4, 4.3	1, 2.2

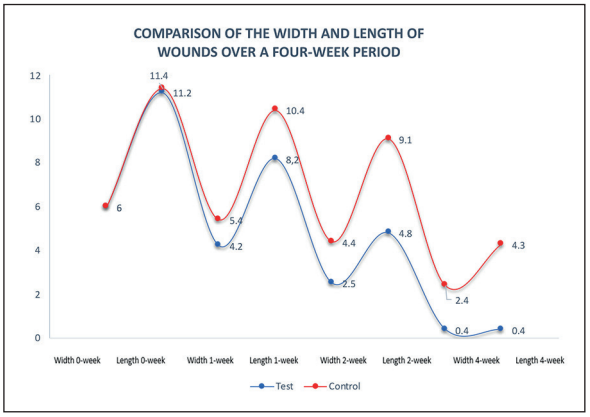

Figure 1. Demonstrates the donor site measurements (Width and Length) in the follow-up period.

and 91% (in length) for test group *vs.* 14% (in width) and 9% (in length) for the control group which the difference being statistically significant (p=0.001). In general, the control group experienced significantly higher pain and discomfort (p=0.001) compared to the test group as shown in Figure 2.

Discussion

Wound healing involves four stages namely: coagulation and hemostasis, inflammation, proliferation and wound remodeling. Honey alters the natural physiological process of wound healing by contributing to some of these stages[16]. It has been reported that honey aids to decrease the exudates and edema from the wounds, as well as it stimulates the epithelialization and granulation process. By this granulation and epithelialization, honey provides the rapid autolytic detriment of wounds which delivers a moist environment to the area of wound and prevents the scar formation[17]. Honey derived from the New Zealand releases tumor necrosis factor alpha (TNF-α) monocytic cells. Moreover, honey increases the production of inflammatory cytokines, such as TNF-α and interleukin-β in the setting of low inflammation, whereas it decreases the production of same cytokines in setting of infection[18]. Furthermore, the pH level (acidic) of honey could stimulate the oxygen off-loading from hemoglobin which ultimately enhances the wound healing[19].

In the present study, a significant decrease in wound site measurements was observed in test group *vs.* the control group, at 1-week appointment (p = 0.001), 2-week appointment (p = 0.002) and 4-week appointment (p =0.001). Healing of donor site percentage was found to be 86% (in width) and 91% (in length) for test group *vs.* 14% (in width) and 9% (in length) for the control group in 4-week appointment, the difference being statistically significant. As for the pain, control group experienced a higher level of VAS (p = 0.001).

Table II. Shows the results of the donor site measurements wound area can be presented in the follow-up period.

Follow-up weeks	Test Group Mean (W, L)	Control Group Mean (W, L)	p* for (w, L)
0-Week (surgery)	6, 11.2	6, 11.4	(0, 0.762)
1-Week	4.2, 8.2	5.4, 10.4	(0.001, 0.028)
2-Week	2.5, 4.8	4.4, 9.1	(0.002, 0.001)
4-week	0.4, 0.4	2.4, 4.3	(0.001, 0.001)

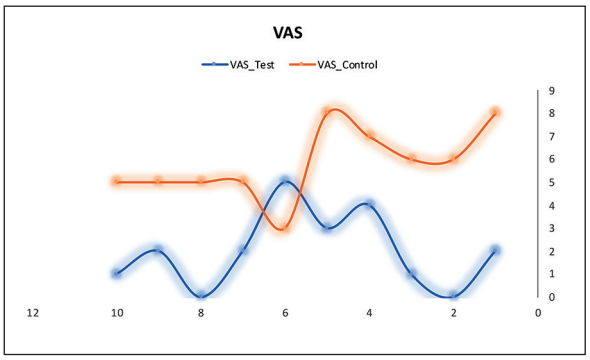

Figure 2. VAS values along follow-up visits for control groups (n = 10) and test groups (n = 10).

A previous randomized trial on Indian Syzygiumcumini honey with Vaseline gauze treatment showed that 48 out of 50 subjects in honey group and 39 out of 50 subjects in Vaseline group achieved epithelialization on day 7. By day 10, 100% subjects treated with honey and 76% subjects treated with Vaseline completely healed[20].

Another study[21] with honey as a wound dressing in split thickness skin graft mentioned that patients reported less pain and discomfort than the previous standard dressing. Moreover, dressing with honey showed lower rate of infection and earlier epithelialization[21]. In the present study the control group experienced a higher level of pain compared to the treatment group.

A Nigerian study[22] with Nigerian Obudu honey reported that experiment group with honey dressing showed more healing compared to the control group at the 5th week of intervention; however, the healing was not statistically significant (p=0.23) at the end of 9th week.

Though the use of honey as a dressing material in surgical wound has been successful in various previous research, some studies[22,23] did not find any significant influence and suggested further clinical trials on using honey as a dressing material.

A study[24] undertaken in 26 centers in Australia and New Zealand exhibited no significant difference with regards to infection prevention of the wound site when Medihoney anti-bacterial wound gel plus was used in comparison to standard wound care.

Honey has also been used in cancer patients earlier. 'Pure natural honey' has been also used in patients who required radiation therapy affected by cancer in head and neck region and observed 41% and 22% reduction of mucositis in grade 3 and grade 4, respectively. On the other hand, no significant difference was perceived in comparative study between manuka honey and placebo gel in treatment with post radiation mucositis in cancer patients[25,26].

One study[27] investigated the healing effect of advanced platelet-rich fibrin (A-PRF) clot membranes in palatal wounds, resulting from FGG harvesting and suggested that A-PRF membranes speeds up the healing process and showed less painful post-operative period.

A systematic review[28] on honey dressing in wound treatment highlighted that honey in acute and chronic wounds provided rapid epithelization and wound contraction in wound healing. It also had anti-inflammatory and debridement effect which decreased the pain and ensured infection control. Along with shorter healing time it was also cost-effective.

Strengths and Limitations

Though many studies validate the use of honey as a dressing material in surgical wound, some studies oppose the idea as no significant influence was observed. Therefore, further studies on honey as a dressing material need to be conducted for better understanding of the clinical benefits of honey in palatal wound healing and the consequent effects in post-surgical morbidity.

Conclusions

The result of this current study suggests that the honey dressing material accelerated the wound healing process of the palatal wound after harvesting FGG. It also showed shorter recovery period along with less post-operative morbidity.

Conflict of Interest

The Authors declare that they have no conflict of interests.

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Ethics Approval and Informed Consent

This prospective randomized case-control study was approved by the Institutional Review Board (IRB) at Ri-

yadh Elm University. The IRB approval number is FP-GRP/2019/438/36/80 and the study was also registered in ClinicalTrials.gov (NCT04269694). The participants were informed about the exact procedure of the study.

Consent for Publication

Written informed consent for publication was obtained from the participants. A copy of the consent form is available for review by the Editor of this journal if requested from the corresponding author.

Data Sharing Statement

The data that support the findings of this study are available from the corresponding author, upon reasonable request.

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Authors' Contribution

MA, AA: Concept; Study design; Intellectual content; Manuscript drafting; NA, AA: Literature search; Data acquisition; Statistical analysis; Manuscript writing KG: Final manuscript approval including editing, reviewing and correspondence.

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