Evaluation of the effectiveness of different biomaterials used for the surgical repair of palatine wounds in gingival grafts

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Gingival thickness is an important factor for periodontium stability, thus playing an important role in preventing gingival recessions. In this context, the free gingival graft (FGG) is used to increase the width of the keratinized gingiva around teeth and implants. The aim of this study was to evaluate the scientific performance of the literature on clinical parameters, such as bleeding time, wound closure, re-epithelialization and postoperative pain after tissue repair, related to the repair of the FGG donor bed. After comparing all the biomaterials included in this study, it was possible to infer that the material that produced the best hemostatic effect was microfibrillar collagen hemostat and oxidized regenerated cellulose, in relation to wound closure in the shortest time, mucograft and CollaCote® obtained the best results, however, the biomaterial that promoted the fastest reepithelization was vegetable oil treated with ozone and those with the lowest VAS score for postoperative pain were CollaCote®, medicinal plant extract and collagen sponge associated with cyanoacrylate.

**Keywords:** Gingival Grafts, Periodontal Wound Healing, Soft Tissue Repair, Biomaterials.
INTRODUCTION

Gingival thickness is important for the stability of the periodontium, playing an important role in preventing gingival recessions. In this context, the free gingival graft (FGG) is used to increase the width of the keratinized gingiva around teeth and implants (BURKHARDT, 2015). Due to its anatomical advantages and the ideal thickness of the tissue, the palatal keratinized mucosa has been proposed as the best donor region for FGG. For this procedure to occur without complications from the donor site, knowledge of the anatomical palatal structures is paramount (DEL-PIZZO, 2002).

The hard palate is formed by anatomical structures, such as the palatine process of the maxillary bone and the horizontal process of the palatine bone, both covered by keratinized masticatory mucosa, in which the underlying connective tissue is composed of a dense lamina propria containing adipose tissue and minor salivary glands (YAPRAK, 2018). The height, length and thickness of the donor tissue to perform the FGG, vary according to the anatomy of the palatal vault, the estimate of the thickness of the mucosa in this region should always be done before removal of the graft. However, some postoperative complications can occur, such as paresthesia, excessive bleeding and difficulties in healing the donor bed (BURKHARDT, 2015).

The wound repair process is an event organized and divided into stages, the first stage, called hemostatic, occurs the wound sealing through a clot formed by platelets and organized in a network of fibrin, fibronectin and vitronectin, subsequently occurs inflammatory phase, which is mediated by inflammatory cells such as neutrophils and monocytes, and finally, there is the tissue regeneration phase, which is characterized by the formation of a highly vascularized granulation tissue, which will later be replaced by a new tissue. The three main cells that are involved in the final stage of the repair process are the endothelial cells, responsible for the formation of blood capillaries, fibroblasts and myofibroblasts, necessary for the formation of new connective tissue and the contraction of the wound and the epithelial cells, that contribute to the re-epithelialization of the place (YAPRAK, 2018).

Difficulties in the repair process can lead to wound dehiscence and the formation of hypertrophic scars, so the closure of the surgical wound must be carefully evaluated and treated (HEO, 2011). Biomaterials have the purpose of repairing or replacing tissues or organs, and must have physical and biological properties compatible with the tissues of the host, in order to stimulate an adequate response. Its indication in different clinical situations must always be well evaluated, taking into account the risks and benefits produced from the analysis of its biocompatibility and biodegradation (WESSEL, 2008; KESKINER, 2016).

The survival and integration of FGG depends on favorable factors, such as the blood supply to the affected tissues and the prevention of bacterial infection. The primary closure
of the wound on the graft biomaterial ensures that the repair takes place in an environment where microorganisms are difficult to enter (THOMA, 2012; KESKINER, 2016).

A variety of biomaterials have been used to cover and protect the wound surface of the palatal donor site after periodontal surgery, showing promising results in healing the site and in postoperative comfort. The aim of this study was to evaluate the scientific performance of the literature on clinical parameters, such as bleeding time, wound closure, re-epithelialization and postoperative pain after tissue repair, related to the repair of the FGG donor bed.

**LITERATURE REVIEW**

According to the reviewed literature, different biomaterials used in the palatal surgical wound were observed, as well as different surgical protocols. In the study by SAROFF (1982), grafts of thickness 1-1.5 mm were obtained using Bard-Parker slides No. 15 in the posterior lateral region of the palate. Two different biomaterials were used, Coe Pak™ periodontal dressing and the microcrystalline collagen hemostat in the surgical wound in each corresponding group, with a clinical follow-up lasting 28 days. Rossmann (1999) measured the dimensions of the donor tissue wounds in terms of length, width and thickness, using a standard periodontal probe, subsequently applying different biomaterials, such as oxidized regenerated cellulose and absorbable gelatin sponge, to the patients for 21 days.

In the study by YEN (2007), the thickness of the palatal donor tissue was measured using a bone probe with the aid of a surgical guide, the biomaterials used were Coe Pak™ periodontal dressing and platelet concentrate in the different groups, and the mean follow-up time for the patients was 6 weeks. The surgical protocol used by SHANMUGAM (2010) was based on the preparation of the recipient site for the placement of the graft, acquiring a palatal donor tissue in the necessary dimension, the biomaterials used in the surgical wound of the palate were Coe Pak™ periodontal dressing and CollaCote®, with an average follow-up time of 42 days.

In the study by THOMA (2012) two biopsies of 6 mm in diameter and 3 mm in depth were performed, collected from the palate, using a surgical stent and a biopsy punch and subsequently, the biomaterial Mucograft ® was applied at the donor site and the patients were followed for 29 days. PATEL (2012), in their study, did not describe the surgical protocol adopted, however, the biomaterials used in the surgical wound of the palate were non-ozoneated oil and olive oil treated with ozone, with an average follow-up time of 18 months.

KECELİ (2015) carried out a surgical protocol, based on making a rectangular incision with 1-1.5 mm thick on the palate, using later on the surgical wound of the donor site, extracts of medicinal plants, following the patients for 6 months. FEMMINELLA (2016) performed a measurement in the median palatal position, 5 mm apical from the gingival margin of the
first premolar, using an endodontic reamer. The reamer was inserted perpendicularly to the mucosal surface through the soft tissue, with light pressure until the hard surface was felt. The silicone disk was then placed in contact with the surface of the soft tissue through a drop of cyanoacrylate, and after careful removal of the reamer, the penetration depth was measured with a calibrator, with an accuracy of 0.1 mm. The biomaterials used in the surgical wound of the palate were platelet-rich fibrin and gelatin sponge and the average follow-up time was 4 weeks.

In the study by USTAOĞLU (2016), the donor area was extended from the angle of the distal canine line to the angle of the mesial line of the maxillary first molar, using the conventional technique through the scalpel incision, a graft of approximately 1.5 mm. rectangular thickness and shape was obtained. The collection of grafts from the same location in all patients resulted in a uniform technique to compensate for differences in healing of the molar and premolar areas. The biomaterial used was platelet-rich fibrin associated with titanium particles (T-PRF), with an average follow-up time of 6 months. YAGHOBEE (2018) used a graft collected from the premolar and first molar area of the hard palate. A wound area 1.5 mm deep was created at the donor site, measuring 10 × 15 mm, afterwards the gel containing erythropoietin and the gel that did not contain erythropoietin were used as the biomaterial of choice, with an average follow-up time of 28 days.

TAVELLI (2019) measured the thickness of the palatal tissue in the mesial, central and distal parts of the area designated for graft collection, using the same anesthesia needle, containing an adjustable silicon disk stop. These measurements were performed approximately 2 to 3 mm apically to the gingival margin of the adjacent tooth. The biomaterials used in the surgical wound of the palate were hemostatic collagen sponge and collagen sponge sealed with a bio-adhesive material (cyanoacrylate), and the mean follow-up time was 14 days.

The SAROFF study (1982) revealed that microcrystalline collagen hemostat is an effective topical hemostatic substance, with an average hemostasis time in the surgical wound of one minute, while Coe Pak™ periodontal dressing has an average hemostasis time of 20 minutes. ROSSMANN (1999) used two types of biomaterials in their study in their study, namely, the oxidized regenerated cellulose and the absorbable gelatin sponge. In the control group, only one understanding was performed on the surgical wound with sterile gauze. Regarding the hemostasis time, a better result was observed when using the absorbable gelatin sponge in the surgical wound, whose bleeding time was 2 minutes, but the oxidized regenerated cellulose produced a bleeding time of 4 minutes. However, both experimental groups showed hemostatic results superior to the control group, whose bleeding time was 9 minutes.

KECELI (2015), in their study, used different medicinal plant extract in the surgical palatal wounds of the experimental groups, however, in the control group, only a compression with
sterile gauze was performed. The authors observed that the different medicinal plant extracts produced better hemostatic results in surgical wounds, with a bleeding time of 3 minutes, when compared to the compression performed with gauze, whose bleeding time was 5 minutes.

Regarding the closure of the surgical wound and the re-epithelialization of the donor site, different results were observed associated with the use of different biomaterials. In the study by SAROFF (1982), both groups studied showed total wound closure, as well as a complete re-epithelialization of surgical wounds from the palatal donor sites in 28 days, no significant differences were also observed between the biomaterials used. In the ROSSMANN (1999) experiment, only the experimental groups studied showed a complete re-epithelialization of the surgical wounds in 21 days. With regard to the total closure of surgical wounds, only the group that used oxidized regenerated cellulose showed significant results.

YEN (2007) observed complete re-epithelialization and total closure of surgical wounds in 6 weeks, when using platelet concentrate, which differs from the control group, which used the placebo, presenting incomplete re-epithelialization and wound closure in 6 weeks. SHANMUGAM (2010), in their study, compared the effectiveness of Coe Pak™ periodontal dressing and CollaCote® in the processes of re-epithelialization and total closure of surgical palatal wounds. These authors observed the total closure of the wounds in 7 days, using only CollaCote®. The re-epithelialization of surgical wounds was evaluated over a period of 42 days, and complete re-epithelialization was observed in both groups.

THOMA (2012), evaluated only the action of Mucograft® as a biomaterial used in the surgical wound of the palate. Total wound closure was observed in 8 days when using Mucograft®, however, in the control group, there was no total wound closure in the total follow-up time. Complete reepithelialization was also noted in the 29-day period in both groups. PATEL (2012) used olive oil treated with ozone and non-ozonated oil in their palatal surgical wound in their study. It was observed in both groups, the total closure of the surgical wound in 21 days. It was also noted that in the experimental group it was possible to observe complete reepithelialization of the surgical palatal wound in a period of 7 days, which did not occur in the control group in that same period.

KECELI (2015), observed that the groups treated with the different types of medicinal plant extract presented a complete closure of the surgical wounds, with complete epithelial reepithelialization in the period of 4 weeks, however, the control group presented an incomplete closure and reepithelization of the surgical wound. during the studied follow-up period.

FEMMINELLA (2016), in their study, compared the use of platelet-rich fibrin and gelatin sponge in surgical wounds on the palate. Total closure of the surgical wound was observed, for both groups of patients, in a period of 4 weeks. The study also showed that the gelatin sponge showed a better result in reepithelialization, favoring a complete reepithelialization in
the period of 3 weeks, when compared with platelet-rich fibrin, which presented incomplete reepithelialization in that period.

USTAOĞLU (2016) used, in their study, a combination of platelet-rich fibrin associated with titanium particles (T-PRF) and compared it with a control group, which used only compression with sterile gauze on the surgical wound of the palate. The authors observed that only the experimental group had total wound closure at the donor site in 21 days. It was also observed that the group treated with T-PRF reepithelialization was complete in 14 days, differing from the control group, which did not present complete reepithelialization in that period.

YAGHOBEE (2018) compared the use of gel containing erythropoietin and gel that did not contain erythropoietin in the palatal surgical wound. Total wound closure was observed in 28 days in both groups analyzed. In addition, the authors observed that the group that used the gel containing erythropoietin in the donor site, the period of complete reepithelialization was 3 weeks, differing from the group treated with the gel that did not contain erythropoietin, whose period of reepithelialization was longer.

In the study by SAROFF (1982), all patients had postoperative pain, which gradually decreased over time and there was no significant difference in relation to pain in the surgical wound between the groups evaluated. Rossmann (1999) and YEN (2007) also found no significant differences with regard to postoperative pain between studied groups.

SHANMUGAN (2010) evaluated the parameters related to pain using the Visual Analogue Scale (VAS), and observed that patients who used CollaCote ® on the surgical wound of the palate had a lower pain score on day 2 when compared to the control group. However, there was no difference between groups on day 7. THOMA (2012) did not observe significant differences in relation to postoperative pain in the groups studied.

KECELI (2015) in their study, observed that during 6 days, the pain scores evaluated through the VAS were significantly higher in the patients in the control group when compared to the groups that used medicinal plant extract, in the other days there were no significant differences between the experimental and control groups. FEMMINELLA (2016) and USTAOĞLU (2016) did not observe significant differences in the occurrence of postoperative pain in the groups studied. TAVELLI (2019) observed in their study that patients who used collagen sponge associated with cyanoacrylate had a lower postoperative pain score, when compared with the control group, being confirmed by VAS.

### DISCUSSION

The ultimate goal of periodontal surgery is to recreate the structure, function and aesthetics of the tissue (WINDISCH, 2019). FGG is a treatment modality used to increase keratinized gums, prevent / treat gingival recession, improve aesthetics, reduce or eliminate root
hypersensitivity, among other functions. However, after graft harvesting, it takes approximately two to four weeks for the wound developed during the harvesting of donor tissue to heal, as a result, patients experience postoperative pain, excessive bleeding and discomfort during the initial healing phase (SILVA, 2010).

The morbidity associated with the healing process of the donor site has been a major concern in the clinical dental routine, factors such as graft thickness are directly associated with the degree of morbidity. The present study compared the use of biomaterials to repair the donor site in FGG, demonstrating that their use helps in the process of repairing the donor site of FGG, taking into account parameters such as bleeding time, wound closure, re-epithelialization and loss of sensation after tissue repair. The SAROFF study (1982) demonstrated that the collagen hemostat microfibrillar, by acting as a stimulus for platelet adhesion, forming a fibrin network, promotes hemostasis in a time interval of less than 1 minute, when compared with the other studied biomaterials.

SAROFF (1982) and SHANMUGAN (2010) observed that biomaterials such as CoePakTM, a periodontal surgical cement, produce hemostasis only after 20 minutes of application, this biomaterial, although free of eugenol and, therefore, does not present irritating substances, has little biological effect. in the palatal tissues, which would justify a longer time necessary for the production of its hemostatic effect, not presenting itself as a biomaterial of choice, if the purpose of its use is to promote the hemostasis of the surgical wound.

In the study by ROSSMANN (1999), there was an influence of smoking habits in the postoperative evaluation, with smoking patients having a shorter bleeding time than non-smokers. This situation can be explained, probably, by the nicotine vasoconstrictor effect, which promotes a rapid hemostasis when compared to nonsmoking patients. Patients who used oxidized regenerated cellulose obtained a hemostasis time, on average, of 2 minutes for non-smokers, while smokers obtained an average time of 1 minute. Regarding the use of absorbable gelatin sponge, its action was intermediate in relation to the three groups tested in this clinical trial. Although its action is not completely elucidated, this fact is justified by helping with coagulation, forming a mechanical matrix under the surgical wound.

Regarding the healing process, YAGHOBEE (2018) observed that the gel containing erythropoietin improves the healing of palatal wounds during the third and fourth weeks following free gingival graft procedures. Positive effects of EPO on wound healing have been demonstrated in several in vivo studies. BUEMI (2004) showed in their study that the gel containing erythropoietin administered subcutaneously significantly advanced the early and late stages of wound healing in healthy rats, stimulating angiogenesis and reducing inflammation. In another study, they attributed these effects to the increase in vascular endothelial growth factor (VEGF) and to the development of collagen (BUEMI, 2002).
SHANMUGAN (2010) pointed out in their study, that CollaCote®, being based on collagen that is a natural substrate of the extracellular matrix, promoted a faster and more complete cure (7 days) than the control group (Coe-Pak), the collagen used in the study is predominantly of type IV and I, and type IV is conducive to reepithelialization and accelerated healing.

Mucograft also presented a satisfactory result in the study by THOMA (2012). In this study, the use of Mucograft (test group) was compared with a control group that received no additional treatment at the donor site. After 4 and 8 days, it was observed that the surgical wound in the experimental group exhibited a smaller size when compared to the control group. After 15 and 29 days, the results were statistically similar between groups. The xenogen collagen matrix, the main component of Mucograft, can serve as a blood clot stabilizer, in addition to forming a kind of framework for the development of the extracellular matrix and the formation of connective tissue, a fact that justifies its faster action than the control group.

Biomaterials behaved in different ways with regard to reepithelization, biomaterials, such as Coe Pak™ surgical cement, had a reepithelization time of around 6 weeks, which could be justified by their low tissue biocompatibility or the fact that they act as an important biofilm retainer, hindering the process of repairing the surgical wound of the donor bed. Similar results have been found in other biomaterials such as absorbable gelatin sponge and platelet concentrate.

In the study by PATEL (2012) it was observed that the vegetable oil treated with ozone, presented the best results, producing a complete reepithelization of the surgical wound in about 7 days. Considering that reepithelialization constitutes a stage in the wound healing process, in which there is an interaction between several growth factors, cytokines and cell cycle regulators, ozone acts precisely on this process, being related to the stimulus of oxygen metabolism.

The study by BOCCI (2018) demonstrated that the mechanism of action of ozone is related to an increase in the rate of glycolysis of red blood cells, which increases the stimulation of 2,3-diphosphoglycerate, causing an increase in the amount of oxygen released to the tissues, thus stimulating the production of interferon and decreasing the tumor necrosis factor and interleukin-2, minimizing the intensity of immunological reactions, favoring a rapid healing of tissues. In addition, the oxygen present in ozone, once inside the donor bed, can act as a local antimicrobial, especially with regard to fighting anaerobic bacteria, interfering with microbial colonization on the wound surface, thereby reducing the inflammatory process, the formation of granulation tissue and therefore speeding up the wound repair process.

Regarding postoperative pain in the donor bed, some biomaterials have minimized this discomfort. In the study by SHANMUGAM (2010) patients who used CollaCote® on the surgical wound of the palate had a lower pain score on the second day when compared to the
control group, these results may be justified, due to the fact that CollaCote® is composed by a sterile, bioabsorbable collagen protein matrix of animal origin, designed to provide an occlusive coverage of the surgical wound, keeping the environment clean for healing to occur.

KECELI (2015) em seu estudo, observaram que os grupos que utilizaram medicinal plant extract, apresentaram um escore VAS menor de dor durante os 6 dias. In the study by SHANMUGAN (2010) it was demonstrated that the use of extracts of medicinal plants is an excellent alternative for the treatment of wounds, minimizing post-surgical morbidities, knowing that some extracts have anti-inflammatory and analgesic properties.

TAVELLI (2019) performed a comparative analysis of the effects of hemostatic collagen sponge and collagen sponge associated with cyanoacrylate in the graft donor sites on the palate, with the aim of minimizing postoperative pain after tissue harvesting. The authors noted that postoperative pain after harvesting palatal tissue can be successfully minimized if the wound opened at the donor site is protected with an outer layer of cyanoacrylate on a collagen sponge.

CONCLUSIONS

After comparing all biomaterials included in this systematic review, according to the four parameters analyzed, bleeding time, wound closure, re-epithelialization and loss of sensation after tissue repair, it was possible to infer that the material that produced the best hemostatic effect was microfibrillar collagen hemostat and oxidized regenerated cellulose, in relation to wound closure in the shortest period of time, mucograft and CollaCote® achieved the best results, however, the biomaterial that promoted the fastest reepithelization was vegetable oil treated with ozone and who had a lower VAS score for postoperative pain were CollaCote®, medicinal plant extract and collagen sponge associated with cyanoacrylate.

It is important to note that complete sealing and protection of the surgical wound is the main reason for less postoperative morbidity in the test groups compared to the control groups, observed in this systematic review. The use of biomaterials that contemplate the sealing of the wound associated with the induction of the healing process of the donor area are promising candidates for clinical use.

REFERÊNCIAS


