EUROPEAN JOURNAL OF BIOMEDICAL AND PHARMACEUTICAL SCIENCES
http://www.ejbps.com

ISSN 2349-8870
Volume: 8
Issue: 3
115-120
Year: 2020

MANAGEMENT OF COMPLICATIONS FOLLOWING GUIDED BONE REGENERATION TECHNIQUE

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Article Received on 21/12/2020 **Article Revised on 19/01/2021** **Article Accepted on 09/02/2021**

GBR has shown high long-term success rates (implant survival rates) that are similar to implant placement in pristine bone based on high evidence level publications. Moreover, it has been demonstrated that these success rates are achieved whether GBR is applied in a simultaneous or staged approach.[1] GBR is an alveolar ridge augmentation technique that has been shown to produce excellent, reproducible results. GBR uses a membrane (resorbable or nonresorbable) and with or without a graft materials beneath the periosteum to create and maintain a space around the bony defect where new bone can grow. Since osteoprogenitor cells grow relatively slowly, the membrane separates the maintained space from rapidly proliferating epithelial and connective tissue cells, preventing their migration into the defect.[2]

A number of factors have been implicated or shown to adversely influence periodontal regeneration therapy. These include bacterial contamination, smoking, diabetes, defect morphology and tooth anatomy, membrane exposure, gingival thickness and space maintenance.

FACTORS AFFECTING SUCCESSFUL REGENERATION

1. Bacterial contamination:

It is well established that plaque control is a critical determinant of the success or failure of various outcomes of periodontal therapy. Guided bone regeneration sites during the active healing phase were more likely to be colonized by periodontal bacteria than sites treated without membranes.

The fact that most GBR failure occur in patients with severe periodontal disease is probably due to periodontal pathogens that colonize the membranes from periodontal lesions, which can induce an inflammatory reaction and prevent heaing. The harmful effects of such bacteria in GBR can be a result of virulence factors. *P.gingivalis* elaborates collagenases and other proteolytic enzymes. *A.actinomycetemcomitans* has a fibroblast inhibitor and other toxins that can induce tissue damage. In clinical sites with submerged barrier membranes, periodontal pathogens are not present, whereas high proportions of *P.gingivalis*, *A.actinomycetemcomitans* and *Peptostreptococcus micros* have been found in exposed membranes coupled with minimal bone regeneration. Hence exposed membrane is associated with high risk of bacterial contamination and has a negative influence on periodontal therapy. The recommended use of antimicrobial treatment aims at suppressing periodontal pathogens prior to membrane placement and maintaining a healthy environment during the healing period.[3]

2. Smoking

Smoking reduces vascularization and has a negative influence on the microcirculation of the tissue, leading to flap necrosis and dehiscence, with exposure of the bone graft. Nicotine induces modification in plasma constituents and compromises neutrophil functionality. Smoking promotes bacterial development of organisms such as *P.gingivalis*, *P.intermedia* and *A.actinomycetemcomitans*. Chronic smoking possesses a high chance of failure of the regenerative therapy. In a retrospective analysis of a longitudinal study of GTR procedures in class II furcations, Rosenberg et al reported a 42% failure rate after at least 4 years. Of those failures, however, 80% were in patients who smoked at least 10 cigarettes per day for 5 years. Smoking produces a 4.3 times increased risk of an unfavorable response.[4]

3. Diabetes

Diabetic patients with less than optimal glucose control should be at increased risk for failure with regenerative procedures. There are high risks of protracted wound

healing and postoperative infection caused by functional deterioration of leucocytes, decreased collagen metabolic capacity, deteriorated function of fibroblast cells to repair tissues, and poor circulation caused by microcirculatory disturbance. Improved metabolic control is currently the only practical approach to manage this risk factor. There are currently no data to quantify the influence of diabetes on the success of regeneration. Since patients with diabetes have a high risk of infection, it is important to provide tight plaque control and glycemic control in periodontal treatment. Schwartz-Arad et al in 2005 determined the presence of diabetes to be a risk factor for failure in regenerative procedures, citing lower success rates of block grafts in patients known to have diabetes.[5]

4. Defect morphology and tooth anatomy

The number of associated bony walls and overall defect depth has long been related to success of regenerative therapy. In a retrospective analysis of 26 proximal defects treated with flap surgery and e-PTFE barrier membranes, Selvig et al in 1990 concluded that the extent of crestal involvement, circumference, number of tooth walls involved, and wall form in the fundus of the defect did not influence the healing response. Attachment gain and bone fill were positively correlated with the depth of the 3-walled intraosseous component of the defect.[6]

Tonetti MS, Pini-Prato G et al 1996 in a series of study focused on factors affecting healing of intraosseous defects treated by GTR also identified increased total depth of the intraosseous component of the defect as well as decreased radiographic width of the defect angle as important positive correlates of regeneration. The decreased amount of regeneration associated with an increased radiographic defect angle between the root surface and defect wall may reflect space loss and clot disturbance caused by postoperative collapse of the membrane. The greater distances required for cellular repopulation of the wound or an enhanced susceptibility to oral environmental factors may lead to incomplete bone fill. The oral environmental factors, including mechanical trauma and infection, are also proposed as primary reasons for incomplete fill of the most superficial portion of the defect.[7]

5. Membrane Exposure

The most frequent postoperative complication of GBR is membrane exposure. One cause of early membrane exposure is necrosis of a thin flap covering the membrane. In GBR, blood supply to the flaps depends on flap thickness because blood supply from the bone to the flap is impeded by the membrane. In a meta-analysis conducted by Machtei et al[8], they reported an overall incidence of membrane exposure of 60% in GBR procedures. Membrane exposure during healing had a major negative effect on GBR around dental implants. Early membrane exposure is a common problem in GBR during fixture placement, but it does not mean treatment failure.[9,8] Thus membrane exposure due to postoperative soft tissue dehiscence is disadvantageous, but thorough postoperative oral hygiene helps counter the problem as it reduces the likelihood of infection.

6. Gingival thickness

The thickness of the flap covering the membrane is an essential consideration.

To maintain blood supply to the flaps, to prevent flap necrosis, and to achieve favorable results, more than 1.5 mm gingival thickness is a prerequisite. If GBR is performed in deep osseous defects with thin gingiva in the maxillary anterior region, recession of the interdental papilla or gingiva will occur.

7. Space maintenance

Space maintenance is considered a desirable property in a barrier device, with a direct correlation between bone volume regenerate and potential volume beneath a membrane**.** Bone can be regenerated within localized alveolar ridge defects using a flexible, titanium-reinforced e-PTFE membrane that can be shaped to conform to the desired ridge morphology with the purpose of preventing membrane collapse within the ridge defect. In addition to membrane rigidity, other means of providing space maintenance includes the use of tenting screws, osseous particulate grafts, corticocancellous osseous block grafts, dental implants, and use of binding agents in combination with osseous graft materials. In cases where these membranes are used to treat ridge defects, graft material is placed into the ridge deformity to support the overlying collagen membrane, thus facilitating space maintenance.[9]

COMPLICATIONS & MANAGEMENT

The postoperative healing after GBR procedures with e-PTFE or non resorbable materials is physiologically different from the healing that occurs after replaced flap techniques. The postoperative blood supply to the flap in a conventional replaced flap procedure is derived from the base of the flap, the underlying bone, the periodontal ligament space and newly formed periosteum. Neovascularizarion of the gingival flap from vessels within the osseous tissues and bone-periosteal surface is blocked by GBR membranes. This prevents establishment of critical collateral microvasculature anastomoses necessary for gingival flap survival. Blood perfusion studies have demonstrated that blood flow to the coronal edges of the mucosal flap is significantly decreased after a GBR procedure compared to the blood flow allowed by a replaced flap procedure. This altered neovascularisation of the healing flap is fundamental to most of the postoperative complications of GBR.

In periodontal applications, by 4 weeks of healing, a small portion of the coronal aspect of the e-PTFE membrane is often exposed, and a space lateral to the e-PTFE barrier is created. This space or "pseudopocket" can be the site of bacterial colonization and abscess formation. In GBR procedures exposure of the

membrane is common and introduces variability to the healing response.

The most problematic and common complication is soft tissue dehiscence of the mucosal flap. Abscess formation can also occur in areas of small perforations. Soft tissue dehiscence usually occurs near a crestal incision site or adjacent to a proximal tooth surface. The chance of soft tissue dehiscences increases when GBR is done in conjunction with immediate implant placement in extraction sockets.

Postsurgical complications associated with guided bone regeneration (GBR) techniques, for bone augmentation alone or in association with implant placement are:

1. Pain.
2. Swelling.
3. Purulence or abscess formation - Suppuration or the presence of an unclear exudate in the space external to the membrane.
4. Sloughing - The postoperative reduction or recession of the flap height of greater than 4 mm.
5. Exophytic tissue - Rapidly growing granulation tissue that grows past the barrier membrane. It may bleed spontaneously.
6. Perforation of flap & Membrane exposure - An exposure of the membrane through the mucosal flap at the apical border of the membrane.

TREATMENT OF COMPLICATIONS

Pain

The current approach for both long and short term pain relief is to provide the patient with pain medication immediately after treatment, before any pain is felt. Long to medium term acting anesthetic agents such as Ultracaine Forte (1:100,000 epinephrine) can control pain for up to 4 hr after the procedure. Antiinflammatory agents such as Ibuprofen (400 mg) or Dexketoprofen (25mg) may be taken just before the surgery. These non steroidal anti-inflammatory agents block the formation of prostaglandins, which in turn stimulate the release of substances causing a pain cascade. Blocking the pain response before it begins results in much shorter or even no postoperative pain episodes. As postoperative pain is usually most severe the night of and the day after surgery, the patient should continue the pain medication through the second and if needed the third day too.

Swelling

Swelling is a normal surgical sequel, but is a cause of great concern to the patient. For this reason the patient must be informed that the surgical site or the face may swell, regardless of home care. Application of mild cold packs must be used in intermittent protocol for 2 days. The IV administration of glucocorticoid steroids e.g., prednisolone 250 mg or dexamethasone 8mg may also be considered prior to surgery.

Hematoma can complicate and prolong the post operative phase. Hematoma can be identified by palpation as a non-sliding induration, which is painful to pressure. Excessive swelling may require antibiotic prophylaxis if not already ongoing.

Purulence

Purulence occurs only at sites that demonstrate material exposure. However, in many sites that demonstrate purulence, associated gingival tissues present with only mild gingival inflammation. Because only sites that demonstrate material exposure display purulence, the presence of purulence appears to be dependent on the development of the pseudopocket, or gingival space, lateral to the BM. Once this pseudopocket is present, purulence is related to the length of time that the material is allowed to remain in place. Given that most GBR surgical sites will develop material exposure, prevention of purulence is related to timely removal of the material within 4 to 6 weeks. The manufacturer recommends that the material be removed at 4 to 6 weeks, and this guideline is consistent with prevention of the purulence complication. However, removal of material at this recommended interval may decrease the regenerative result if the newly regenerated tissues have not yet fully matured and will not survive intact in the oral environment.

Microflora

Bacteriologic studies of purulent or abscessed sites associated with periodontal applications reveal that the morphotypes of the purulent sires are predominantly cocci and nonmotile rods, constituting 46.2% and 49.1% of the flora, respectively Spirochetes accounted for 1.7% and motile rods accounted for 2.9%. The most common species cultured were *Streptococcus* and *Actinomyces* species. *Prevotella intermedia* and enteric flora was also found. Half of the purulent sites display some form of antibiotic resistance to penicillin, tetracycline, or metronidazole. Purulent areas respond to home irrigation devices using tap water and the administration of a systemic antibiotic. In the event of abscess formation, amoxicillin with clavulanate potassium, 250 mg, three times daily for 10 days, is prescribed. If the patient is allergic to penicillin, or if enteric bacteria arc cultured, ciprofloxacin hydrochloride 500 mg- twice daily for 10 days, is prescribed. Because of this risk of super infection, the use of GTR procedures in systemically ill patients or those who require antibiotic premedication for routine dental procedures has to be critically evaluated. The flora associated with GBR membranes in abscessed or purulent sites is similar to that of samples in non abscessed sites. The predominant flora of the purulent sites is *Actinomyces* and *Streptococcus* species. These are usually associated with normal gingival health or gingivitis.

Treatment of Purulence

Irrigate with chlorhexidine rinse

- Decide if membrane removal is appropriate

- Culture the site if the membrane is to be left in place for more than 3 weeks
- Prescribe systemic antibiotics.
- Recommend home irrigation with chlorhexidine

Exophytic Tissue

The occurrence of exophytic tissue is rare. This reaction usually presents within the first 3 weeks of postoperative healing. These areas are treated by incisional biopsy.

Sloughing of the Gingival Flap and Exposure of the Membrane

In GBR, beveled flap edges and remote incisions help to reduce membrane exposure. Releasing the flap from the underlying periosteum will often allow passive coronal repositioning of the gingival flap and decrease the amount of tension applied to the flap during suturing. Trimming the lateral borders of the membrane exclusive of the open microstructure portion will result in a configuration resembling an apron. Sling suturing through the flexible open microstructure will allow apical repositioning of the membrane. For integration of the membrane into the flap, the flap should be kept 3 mm above the open microstructure portion of the membrane. Treatment of exposed periodontal sites involves supportive care to the patient until the membrane is removed. Chlorhexidine rinses have been suggested but have never proven to affect regeneration when good mechanical oral hygiene is instituted. If the exudate associated with membrane no longer remains clear, the membrane should be removed. Alternatively, Valentini et al have suggested replacement of the membrane if it becomes exposed. In a limited series of case reports, they described significant gains in alveolar bone volumes after placement of second membrane.

Apical Perforation of the Mucosal Flap

Perforation of the mucosal flap occurs in areas where thin alveolar mucosa is laid over sharp osseous contours. Perforation is related to the tendency of the GBR membrane to return to its original shape after the surgical placement of the material. If the BM, which is flat in its original contour, is placed over a sharp osseous crest, the BM will exert a force on tile mucosa in an effort to return to its original shape. This force will often result in perforation of the thin mucosa. Perforation usually occurs between 2 and 5 weeks postoperatively. Prevention of this complication can be achieved by bending or contouring the BM under a gentle tensile force into a shape that will lie passively over the bone defect and the sharp contours of the adjacent alveolar bone. Inadvertent folding of the apical corners of the BM frequently results in mucosal flap perforation. Resorbable membranes are less likely to result in this complication.

Soft tissue dehiscence and membrane exposure

Membrane exposure caused by variable amounts of flap sloughing during healing has been a frequent postsurgical complication associated with the use of non-resorbable membranes. Exposure rates as high as 31% resulting in GBR failure have been reported. Membrane exposure permits a communication between the oral environment and newly forming tissues, increasing the potential for infection and decreasing the likelihood of regeneration.

Clinicians often remove BM (4 to 8 weeks) if exposure occurs. What is unclear is whether the compromised bone fill is a result of inflammation secondary to bacterial invasion or the lack of some protective barrier function as a result of the early removal of the membrane. Soft tissue dehiscence does not necessarily imply treatment failure and good bone fill have been demonstrated in flap dehiscent sites.

The major complication of GBR is membrane colonization by pathogens such as *Porphyromonas gingivalis, Bacteroides forsythus, Fusobacterium nucleatum* and *Propionibacterium acnes*. This colonization can occur as early as 3 min after intra-oral manipulation. These pathogens are particularly damaging for bone healing and constitute one of the major factors of post GBR complications. An infected membrane cannot remain covered and is rapidly exposed.

Causes of premature membrane exposure and GBR failure

1. The treatment plan: Several cases of membrane exposure have been reported when the membrane is placed on the day of extraction with or without immediate implant placement, despite important tissue displacement (coronal or lateral flap). It is preferable to delay membrane placement for atleast 6-8 weeks after extraction to avoid the problem of insufficient covering tissue.
2. The surgical protocol: Crestal incision should extend over one or two teeth around the edentulous area to avoid continuous sutures at the lateral borders of the membrane. The membrane should be situated distant (2mm atleast) to the proximal sides of the tooth to achieve complete coverage by the flap without any communication with oral medium.
3. Size and morphology of the bone defect: In cases of extended bone defects and large membranes, exposure risks because of necrosis of overlapping flaps are important. In fact, reduced blood supply of the flap may lead to pathogen growth and postoperative infection.
4. Anatomic limitations: A shallow vestibule can prevent good tucking of the membrane borders. Similarly, the shape and position of the maxillary sinuses or the localization of nerve emergence can interfere with the indication for membrane placement technique.

COMPLICATION DURING IMPLANT INSERTION AFTER AUGMENTATION

Incomplete healing

At the time of implant placement, usually 4 months after the grafting procedure, the remodeling process is still in progress. Even after 7 months, significant amount of non vital bone are found. Revascularization of the graft is the key to its nutrition and regeneration; revascularization of cancellous bone grafts is 10 fold faster than for cortical grafts. The ingrowth of vessels in a $0.5cm^3$ cancellous graft occurs after 1 week. The regenerative potential of the residual ridge is also a key factor. Highly atrophied ridges usually consist of cortical bone, which is not well vascularized and does not provide many cells. These factors can influence the time needed for remodeling of the graft. Clinically poor regeneration can be visualized by poor bleeding because of an inadequate blood supply or by an inhomogeneous structure and colour.

Mobility of the graft

If the graft is not properly integrated, implant placement can loosen the graft. Poor bone regeneration or mechanical irritation by provisional denture is possible reasons. Osteoblasts differentiate to fibroblasts under mechanical load. If mobility of the graft is observed, soft tissue has to be removed, bleeding should be provoked and the mobile fragment has to be rescued with screws to let it heal for another 3-4 months.

Guided bone regeneration techniques have a unique set of postoperative complications. Most complications can be prevented with modifications of the basic techniques. When complications do occur, treatment failure does not necessarily follow, but the predictability of successful regeneration decreases.[10]

SUMMARY AND CONCLUSION

Guided bone regeneration (GBR) is a predictable means of restoring lost osseous tissue. GBR enhances new bone formation in extraction socket defects, horizontal and vertical ridge augmentation, periimplant bone deficiencies and the correction of dehiscence and fenestration defects around implants. It requires excellent surgical skills and is highly technique sensitive.

Bone regeneration occurs predictably following GBR application in recapitulating intramembranous ossification. In addition, the available preclinical and clinical evidence suggests that GBR constitutes a successful therapeutic approach for the treatment of periimplant bone defects and for the preservation of the dimensions and the configuration of the alveolar socket following tooth extraction.

The use of GBR in implant dentistry is common in conjunction with bone augmentation, implant insertion after extraction, and extraction sites with ridge preservation. A layered approach to GBR improves the success rates and decreases the healing time. Trephine bur particulate bone harvesting from the tuberosity and ramus is often used for this technique. The learning curves of these procedures are easier than block bone grafting and the complications are fewer. As a result, nearly all implant surgeons should be able to use GBR as a regular part of a surgical implant treatment protocol.

Furthermore, lateral and vertical bone augmentation of atrophic alveolar ridges before or in conjunction with implant placement can be achieved via GBR application, albeit with varying degrees of success. Carefully designed clinical studies with sufficient statistical power would be instrumental in elucidating the impact of site and patient related factors on the effectiveness and predictability of the GBR treatment. Ultimately, the goal would be to optimize the case selection process and to introduce guidelines in terms of developing the GBR therapeutic protocol.

Today, as clinicians face larger and more difficult, non-space making defects, the issues of soft tissue coverage and complete defect volume regeneration become even more complex.

Future research should focus on:

1. The investigation of the molecular mechanisms underlying the wound healing process following GBR application.
2. GBR application at the molecular level will be of high significance to develop and implement novel therapeutic strategies. (i.e., Tissue engineering, drug delivery and gene therapy).
3. The identification of site and patient related factors which impact on the effectiveness and predictability of GBR therapy.
4. The evaluation of the pathophysiology of the GBR healing process in the presence of systemic conditions and its potential effect on healing.

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