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Review Article

A Regenerative Approach for Management of Peri-Implantitis

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Abstract

Introduction: Peri-implantitis is an inflammatory process at a specific site and infectious disease that causes inflammation in soft tissues as well as bone loss around an osseointegrated implant. The etiology of peri-implantitis depends on the status and condition of the tissue surrounding the implant, the type of implant design, external morphology, degree of roughness, and excessive mechanical load. The most common microorganisms associated with implant failure are Gram-negative anaerobes (mobile forms) and spirochetes, except the etiology, which is a result of mechanical overload. Diagnosis is made on the basis of bleeding and probing depth of peri-implant pockets, suppuration, changes of color in the gingiva of surrounding tissues, and X-ray of the implant region to assess gradual loss of bone height around the implant tooth. Treatment varies according to the case, whether it is peri-implantitis or peri-implant mucositis. The first and most important step in the management of peri-implantitis is to control the infection by surface decontamination, the detoxification of the surface of the implant, followed by regeneration of the alveolar bone. Resective and regenerative techniques are the two surgical techniques available to clinicians to treat peri-implant diseases. Although the variety of investigations present currently that aim to identify the etiology for peri-implantitis, the best approach to treat implant infection is yet not completely clear and has no universally recognized protocol for treatment. A new regenerative approach seems to be promising in managing implant infection.

Aim of the Study: The aim of the present review is to understand the recent regenerative approach for the management of peri-implantitis.

Methodology: The review is a comprehensive research of PUBMED, Crossref since the year 1998 to 2021.

Conclusion: In reconstructive peri-implant therapy, regenerative surgical techniques have shown good efficacy in the management of peri-implant infection and related parameters. Despite ongoing research, there is yet not enough evidence to select a specific grafting material or membrane that would have long-term benefits. No particular surface decontamination treatment can be considered better that can influence the clinical outcomes of regenerative treatment of peri-implantitis. Peri-implant bone defect morphology is an important factor that influences the final outcomes. Regenerative therapies for the treatment of peri-implantitis are confined to specific and selected clinical scenarios.

Keywords: *Peri-Implantitis; Bone Defect; Regenerative Therapy*

Introduction

Peri-implantitis or peri-implant disease is a pathological inflammatory change that occurs in the surrounding tissue of a load-bearing implant. The peri-implant disease has two entities that are peri-implant mucositis and peri-implantitis. Peri-implant mucositis is a reversible inflammatory reaction in the soft tissues surrounding an implant, while peri-implantitis is an inflammatory reaction that occurs along with the loss of supporting bone in the tissue surrounding an implant. The overall frequency of peri-implantitis for selected implant systems is 5% - 8%. According to numerous studies, anaerobic plaque bacteria is the leading microorganism and may have an adverse effect on peri-implant tissue leading to peri-implantitis. Inadequate distribution of the masticatory forces while chewing is another reason directly related to peri-implantitis, which ultimately causes loosening of the artificial supports of the implant, infection of the surrounding tissues further inflammation. Dental implant failure is often related to failure in osseointegration of the implant. It is considered failed if it is mobile, lost, or shows peri-implant bone loss of more than 1.0 mm in the first year and more than 0.2 mm in the second year. In peri-implantitis, there is a loss of bone loss around the implant which eventually leads to the loss of the implant. Therefore, the optimal result of peri-implantitis treatment is the regeneration of the lost implant supporting hard and soft tissues [1-3].

Etiology

Bacterial infections are one of the major causes of the failure of dental implants. Bacterial flora, which is associated with peri-implantitis, are found to be similar to those present in periodontitis. The most common microorganisms associated with failure of an implant are the gram-negative anaerobes, like *Prevotella intermedia, Prevotella nigrescens, Porphyromonas gingivalis, Treponema denticola*, *Aggregatibacter actinomycetemcomitans, Bacteroides forsythus, Fusobacterium nucleatum*, and *Peptostreptococcus micros*. Healthy tissues around the implant play an important role as a biological defense barrier against some of the agents that cause peri-implantitis. If these healthy tissues are destroyed, bacterial contamination spreads directly to the bone via tissue, leading to its vast and rapid destruction. When a non-noble metal material is connected to a titanium implant, mechanical stress and corrosion can occur; apart from this, a poor design of the implant is another important factor that is to be considered for the development of peri-implantitis. Other systemic etiological factors and risk factors are osteoporosis, diabetes mellitus, smoking, long-term treatment with corticoids, radiation, and chemotherapy [4].

Signs and symptoms

The following signs and symptoms are commonly seen in peri-implantitis lesions [5]:

1. Radiological evidence for vertical destruction of the crestal bone, which is saucer-shaped.
2. Vertical bone destruction associated with the formation of a peri-implant pocket.
3. Bleeding and suppuration on probing.
4. Swelling of the peri-implant tissues and hyperplasia.
5. Pain is an unusual symptom, typically associated with an acute infection.

The diagnosis of peri-implantitis needs careful differentiation from peri-implant mucositis, primary failures to achieve tissue integration, and problems lacking an inflammatory component. The diagnostic parameters used for assessing peri-implantitis include clinical indices, peri-implant probing using a rigid plastic probe, bleeding on probing (BOP), suppuration, mobility, peri-implant radiography, and microbiology [5].

Diagnosis

The clinical examination to assess and diagnose peri-implantitis are the same parameters that are used to assess and diagnose periodontal diseases around teeth that are bleeding on probing (BOP), probing depth (PD) suppuration (SUP), and radiographs. A healthy peri-implant status requires the absence of clinical signs of inflammation, such as swelling, erythema, and bleeding on probing (BOP) [6].

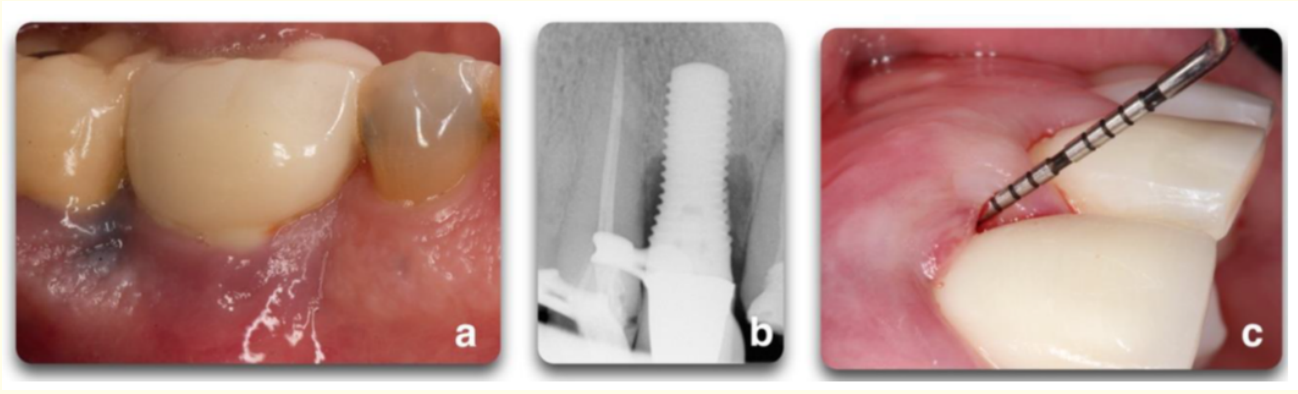

Figure 1*: Shows peri-implant clinical parameters that, associated, can lead to a diagnosis of peri-implantitis. A. BOP/Suppuration, B. radiographic bone level ≥ 3 mm, and C. in combination with PD ≥ 6 mm [8].*

One of the key radiographic pieces of evidence of peri-implant condition is an assessment of crestal bone changes around implants, which helps in differentiating peri-implant health from peri-implantitis. A diagnosis of peri-implant mucositis (PIM) is made if there are signs of inflammation like (BOP, erythema, and soft tissue swelling) whereas when peri-implant mucositis is associated with the progressive loss of supporting bone around the implant, the diagnosis of peri-implantitis (PI) is confirmed. After implant placement and initial loading, 0.5 to 2 mm of crestal bone loss during healing is considered physiological bone remodeling. But bone loss greater than 2 mm after the placement of the implant is suggestive of peri-implantitis. Although the transition of an inflammatory process from peri-implant mucositis to peri-implantitis is not well understood, therefore, it is widely accepted that infectious etiology by the development of biofilm is similar for both diseases. If the lesion around the implant surface remains untreated, further inflammation can lead to progressive bone loss of peri-implant and implant failure. From the time of placement of the implant to the time of disease occurrence and further manifestation, radiographic assessments show a bone level of 3 mm in combination with bleeding on probing, and a probing depth of 6 mm is indicative of peri-implantitis [6,7].

Treatment

Resective and regenerative treatment are the two most common surgical options for the treatment of peri-implant disease. Various methods and treatment approaches have been tested to detect the most predictable outcome for treating peri-implantitis and to reverse, prevent or arrest the loss of bone around the implant. These include either non-surgical methods or surgical resective and regenerative treatments, along with surface decontamination as an adjunctive method. The resective method is the preferred approach when the peri-implant defect is devoid of bone walls or has a supra-bony component [5].

The objective of treating peri-implantitis is re-osseointegration or to fill the osseous defect with suitable bone fill material to provide support to peri-implant soft tissue and thereby improve esthetic outcomes. However, due to varying morphologies of the osseous defect and progressively advancing stages of the disease, these techniques are not always applicable [10].

Re-osseointegration or regeneration events can be assessed histologically in experimental human and animal models. The efficacy of peri-implantitis treatment depends on the outcome of these variables. In terms of clinical protocols are limited to assessments of bone level by clinical variables such as bleeding on probing, probing depth, and radiographs, while experimental protocols also include histological evaluations regarding inflammation resolution and repair of the osseous defect. Re-osseointegration cannot truly assess and be assessed clinically on patients. It can only be analyzed by harvesting histological specimens and their assessment. The other non-invasive

method to assess bone changes after treatment is a radiographic investigation, which is most commonly employed, although it is not a very reliable method to assess treatment outcome by re-osseointegration. Clinically, the most accurate method to identify defect configuration of peri-implant is by direct access during the surgical intervention [9,10].

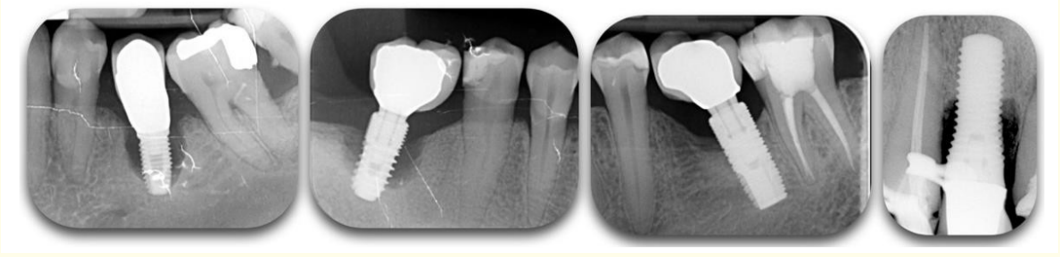

Figure 2: *Showing various bone defects on the radiograph [8].*

Assessment of peri-implant bone defect

Peri-implant bone defect configuration is one of the most important factors related to the success of peri-implantitis regenerative procedures. The regenerative procedures are aimed not at just addressing the resolution of the disease but also at attempting to fill the bone defect created during the disease process. Therefore, to achieve this goal identifying and assessing the bone defect of peri-implant is essential. The type of implant defect and the number of walls surrounding the lesion should be assessed carefully [8].

Figure 3: *The figure shows peri-implant defects according to the number of walls surrounding the lesion. The right corresponds to the number of walls present. The higher the number of walls, the more positive outcomes of regenerative therapy [8].*

A classification of peri-implantitis defects on the basis of intrabony features and horizontal bone loss, the absence of buccal or lingual walls, circumferential and supra- or sub-crestal patterns. It was proposed by Schwarz., *et al*. and verified through intra-surgical findings in animals and humans [11].

To determine the likelihood of success of regeneration therapy in periimplantitis, understanding the peri-implant defect morphology is important. Because for certain situations in which regenerative procedures are unable to or unlikely to produce a favorable outcome,

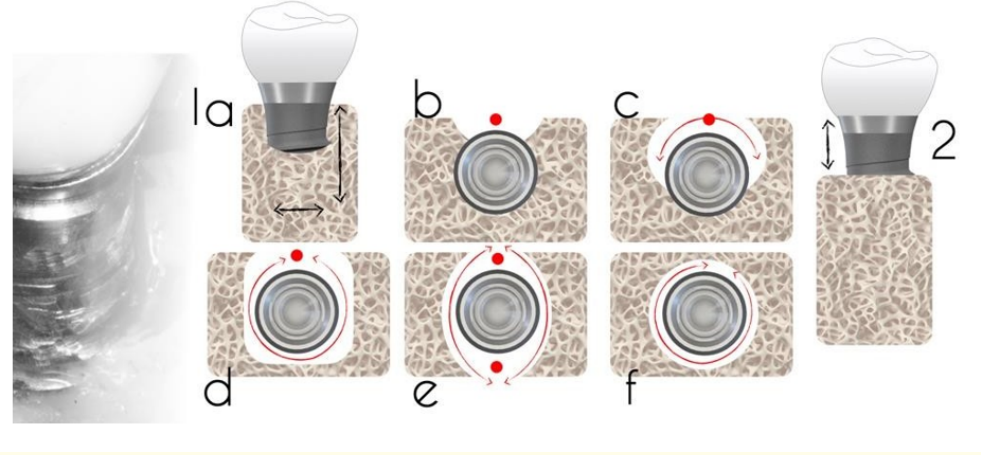

Figure 4: *Shows classification of defect according to an intra-operative assessment (Schwarz et al.).Class 1 - (a) Class 1a-facial view, (b) Class 1a-occlusal view, (c) Class 1b-buccal dehiscence + bone resorption in semicircular form to the middle of the implant body, (d) Class 1c-buccal dehiscence + circular bone resorption with the lingual wall, (e) Class 1d-circular bone resorption with lack of buccal and lingual walls, (f) Class 1e-bone resorption in circular form with the presence of buccal and lingual wall; Class 2 - supra-crestal bone resorption [11].*

resective surgeries are offered and are the choice of treatment. Among all the defect configurations, circumferential defects (Ie) achieved the highest reduction in periodontal depth and clinical attachment level (CAL); the class Ib and Ic defects showed the poorest values. The most prevalent defect is Class I b defects, verified in many studies. Therefore, it peri-implantitis defect morphologies are poorly responsive to reconstructive treatment [12,13].

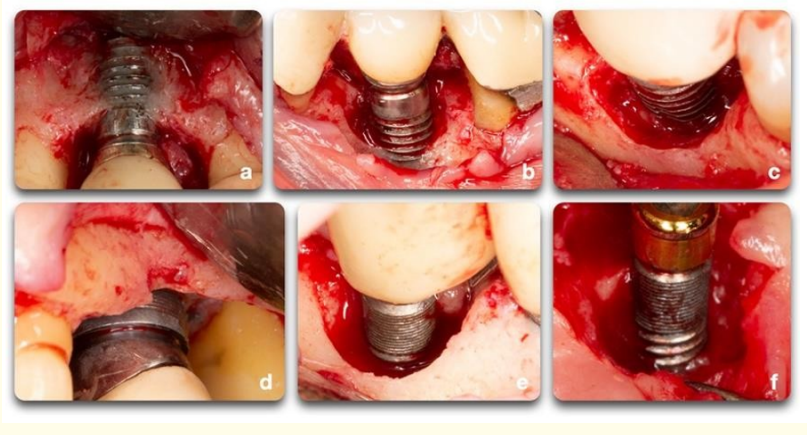

Figure 5: *Shows clinical example of peri-implant bone defects; (A) facial dehiscence, (B, C) semi-circumferential defect and facial dehiscence and (D) supra-crestal bone resorption with circumferential and supra-crestal bone defect [8].*

Surface decontamination - After surgical exposure, various techniques have been proposed for surface decontamination of the implant as follows: chemical, laser or photodynamic, mechanical, or a combination of these. The decontamination process presents various challenges. The implant's rough surfaces and threads pose a significant hurdle in mechanical cleansing. In attempts to solve the infectious process, if not done optimally, can cause pathogenic microflora to reestablish, and there will be a persistence of pathology. Surface decontamination alone is not adequate to achieve bone regeneration in case of advanced peri-implant defect lesions. In advanced peri-implant defect filling, the defect with graft materials and growth factors is required to yield better outcomes [14].

In regeneration techniques, the surface characteristics of the implant also have an impact on the clinical outcome. The complete filling of defect is not always a predictable parameter. The test implant surface sandblasted and acid-etched (SLA) was compared with rough titanium-plasma spray (TPS) control surface; the authors reported that healing was superior with sandblasted, large grit, acid-etched (SLA) test surface implants [15].

The implantoplasty procedure was performed by Nart., *et al.* using allografts mixed with antibiotic vancomycin and tobramycin (1:1) and membranes to fill the defect. The combination of antibiotics showed a positive result in terms of radiographic bone fill, probing depth reduction, and clinical attachment level gain after a period of 12 months. However, in the last studies, the implants treated with implantoplasty removed the surface properties of the fixtures. Therefore, its a matter of debate among the literature whether this procedure should be performed or not [16,17].

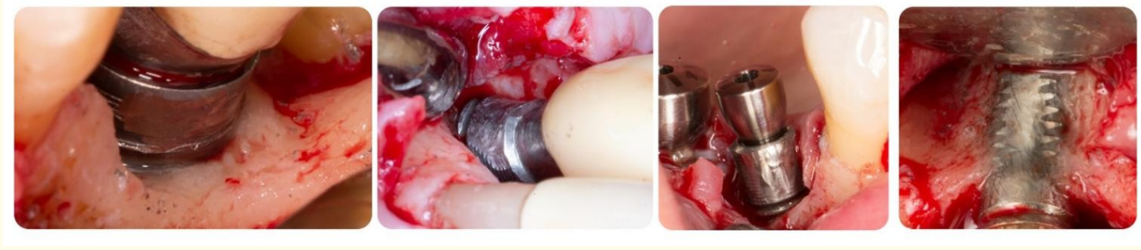

Figure 6: *Figure showing peri-implant surfaces decontamination by means of implantoplasty. The picture represents the difficulty of completely removing titanium debris from the tissues and that it is not possible to completely reach the surface of the implant in narrow defects; implant structure removal is required to gain smoothness. In this way narrower the implant, more is the risk of fracture due to structural modification [8].*

Regeneration techniques and materials

In regenerative procedures of implant defect, there is a reconstitution of the lost attachment apparatus composed of cementum, bone, periodontal ligament, and connective tissue. To validate reconstructive surgical treatment in peri-implantitis, since evidence of reosseointegration can only be confirmed histologically, it should be investigated in pre-clinical trials before applying it to human studies. Due to the ethical considerations on humans, animal studies can be used to determine the successful regeneration of bone around a previously affected implant. Many parameters need to be assessed and controlled, such as scaffold membranes, bone substitute materials, implant surface characteristics, and the process of decontamination, to understand their different roles in re-osseointegration [8].

Schou., *et al*. performed a series of experiments on monkeys with surgical treatment of ligature-induced peri-implantitis. Expanded Polytetrafluoroethylene or ePTFE (Non-resorbable membranes) with xenograft (Bio-Oss) or autogenous bone graft (ABG) were employed. Histologically, both combinations resulted in re-osseointegration (36% in the Bio-Oss group and 45% in the autogenous). The benefits of using membranes and bone grafts were not always significant. as the use of bone substitute materials was not necessary for the resolution of peri-implantitis lesions, bone level gain in radiographs, and occurrence of re-osseointegration [18].

Jepsen., *et al*. used porous titanium granules and reported that the greatest mean defect fills in comparison to other interventions. However, there was no significant difference statistically in bleeding on probing or probing depth. It was concluded that the author's reduction in bleeding on probing was a response to the normal healing process post-surgery rather than the effect of materials used or the method of decontamination applied. The use of porous titanium granules is proven to be the best bone substitute to achieve the greatest radiographic bone level. Followed by Xenograft material, and autogenous bone would come after that. A drawback of evaluating radiographic bone level is that it does not indicate whether the re-osseointegration is complete or not. Since autogenous bone is less radiopaque than titanium granules, it cannot be used to assess comparable radiographic bone levels [19].

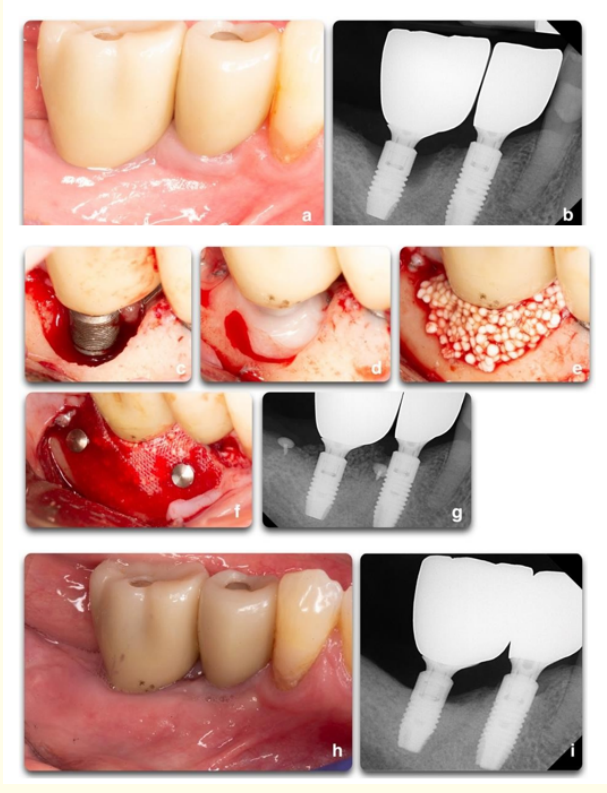

Figure 7: *Figure showing regenerative peri-implant therapy for implant area #31. (a, b) Pre-operative clinical and radiographic presentation. BoP, SUP, PD 10 mm. (c) Defect configuration after the elevation of the full-thickness flap on implant #31. (d) Rotating titanium brushes, chlorhexidine and saline rinse, and the application of PrefGel® 24% EDTA (2021 Institut Straumann AG) for implant surface decontamination. (e, f) Bone grafting application (GUIDOR® easy-graft CLASSIC Alloplastic Bone Grafting System), covered by the GUIDOR matrix barrier membrane and stabilized by two titanium tacks. (g) The grafting material used at the time of surgery completion. (h, i) Follow up after 13 months, post-operative clinical and radiographic outcomes. Partial fill of the intrabony defect with a residual supracrestal defect [8].*

Conclusion

In reconstructive peri-implant therapy, regenerative surgical techniques have shown good efficacy in the management of peri-implant infection and related parameters. Despite ongoing research, there is yet not enough evidence to select a specific grafting material or membrane that would have long-term benefits. Regenerative therapies for the treatment of peri-implantitis are confined to specific and selected clinical scenarios.

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