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Review

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Peri-Implantitis: A Review of the Disease and Report of a Case Treated with Allograft to Achieve Bone Regeneration

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ABSTRACT

Dental implants offer excellent tooth replacement options however; peri-implantitis can limit their clinical success by causing failure. Peri-implantitis is an inflammatory process around dental implants resulting in bone loss in association with bleeding and suppuration. Dental plaque is at the center of its etiology, and in addition, systemic diseases, smoking, and parafunctional habits are also implicated. The pathogenic species associated with peri-implantitis include, *Aggregatibacter actinomycetemcomitans, Porphyromonas gingivalis,* and *Tannerella forsythia*. The goal in the management of peri-implantitis is the complete resolution of peri-implant infection with function. Therapies using various biomaterials to deliver antibiotics have been used in the treatment of peri-implantitis e.g. fibers, gels, and beads. The use of guided tissue regeneration barrier membranes loaded with antimicrobials has shown success in re-osseointegrating the infected implants in animal models. Several uncertainties still remain regarding the management of peri-implantitis. The purpose of this article is to present a background of peri-implantitis along with a case of peri-implantitis successfully treated for bone regeneration.

KEYWORDS: Peri-implantitis; Defect fill; Surgery; Peri-implant mucositis; Bone grafting; Implant failure.

ABBREVIATIONS: GTR: Guided Tissue Regeneration; ePTFE: expanded Polytetrafluoroethylene.

INTRODUCTION

Tooth loss occurs for a variety of reasons and results in resorption of the alveolar ridge if left unreplaced.[1] Achievement of successful periodontal regeneration provides a great challenge to the dental surgeons.[2] Dental implants are a successful in replacing teeth, with implant survival rates reported to be greater than 89% at 10-15 years follow up.[3-5] Around two million implants are placed each year and the number of implants placed per year is expected to increase both due to the success of implant therapies and the aging world population.[6] While success rates of dental implants are initially quite high, 6-12% of dental implants fail and are lost or must be removed.[4,7,8] Failures are due to biomechanical and/or biological imbalances.[6,9-13] High functional loads at the implant–bone interface due to bruxing/clenching or mechanical damage to implant superstructure leads to biomechanical failures.[6,9,12,14] Biological failures are associated with microbial plaque accumulation, bacterial infections, bone loss and sensory disturbances.[6,10,12,15,16] Early biological failures are associated with contaminated surgical implant

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placement or un-favorable healing response.[4,5,10,15] However, late implant failures are typically peri-implantitis, infections induced by plaque.[9,17,18] The consequences of this early or delayed, biomechanical or biological, peri-implant disturbances can lead to loss of implant.[19] Interventional therapies using non-surgical or surgical techniques with or without various biomaterials[1,20-22] and antibiotics have been employed in the management of peri-implant disease to prevent implant failure.[23,24] This article presents literature surrounding peri-implant disease and a clinical case involving a failing implant and its stabilization with allograft bone material.

PERI-IMPLANT DISEASE

Peri-implant disease is an inflammatory process that affects the surrounding tissues of a functional osseointegrated implant.[25] Peri-implant disease is the general term used to describe host tissue inflammatory reactions and is of two types. The first type is peri-implant mucositis which is defined as a reversible inflammatory reaction in soft tissues surrounding the dental implant.[6,26] The second type is the peri-implantitis, defined as an inflammatory process affecting the tissues (soft and hard) surrounding an osseointegrated implant resulting in loss of supporting bone and associated with bleeding and suppuration.[6] Peri-implantitis is usually the result of the disturbance of the equilibrium between the micro-flora and the defense system.[27] The soft and hard tissues surrounding an osseointegrated (bone-to-implant contact) implant shows some similarities with the periodontium in the natural dentition. It is important to realize that the diagnosis of peri-implant disease is not synonymous with implant failure. An infection of the implant does not automatically mean that the implant will fail.[6,10,12,28]

EPIDEMIOLOGY AND PATHOGENESIS OF PERI-IMPLANTITIS

Data from clinical investigations with up to 5 years follow-up show that the incidence of implants exhibiting peri-implantitis is low (0.3-14%) and that the highest incidence of implant loss is within the first 12 months after implantation.[4,5,7,12,29,30] However, this incidence rate could be an underestimation due to poor clinical diagnosis due to avoidance of probing around dental implants during routine clinical exams and the short duration of clinical studies which are less than 5 years. It may take more than 5 years for peri-implant disease to reach clinical expression.[6,10-12,31] Therefore it can be assumed that the incidence of peri-implant disease and implant loss may increase if longer evaluation periods were considered. It has been reported that ~11% failure rate is seen in patients who are smokers versus ~5% for non-smokers, which is attributed to impaired immune function and compromised healing in smokers.[32-35] It has been proposed that smoking cessation before implant placement can result in rates similar to those of non-smokers.[35] Patients with conditions such as osteopenia, osteoporosis, diabetes, hyper-inflammatory phenotype and bisphosphonate use, have been associated with increased risks of implant failure due to poor bone healing and infection.[12] Material surface, properties and design of dental implants also play a role in development of peri-implantitis. It has been observed that exposed rough surfaces tend to accumulate and retain more bacterial plaque than smooth surfaces and are more frequently surrounded by inflamed tissues.[10,36] Calcium phosphate coatings are used to promote osseointegration by increasing the surface area however they increase the risk for peri-implant infection in comparison to non-coated implants.[3,37,38] Peri-implantitis is complex and multivariate with respect to implant design and surface along with patient factors, such as systemic health, smoking, oral hygiene and periodontal disease.[39]

Although bacterial species are known to have complex symbiotic arrangements to optimize survival, changes in composition of plaque microflora such as an increase in acid-producing bacteria or gram-negative anaerobes can lead to diseases such as peri-implantitis.[40-42] Poor oral hygiene results in the development of the bacterial plaque around implants. Maturation of plaque (peri-implant pathogens evolve) contributes to inflammatory infiltrate formation in mucosal tissues, also known as perimucositis.[43] After implantation (in patient with periodontal disease), bacteria move from periodontal pockets of remaining teeth and other oral tissues to colonize the implant surfaces.[9,44,45] Colonization of the implant starts at surface irregularities (supra-structure/ implant collar) and spreads down the implant towards the base.[10] A deficient implant-abutment interface also provides a favorable site for bacterial accumulation, which contributes to the peri-implant inflammatory reactions.[38,46] Although the periopathogenic species in periodontitis and peri-implantitis are almost similar, there are differences observed with respect to relative numbers and species present.[40,47-50] Surviving and successful implants are observed to be populated with gram-positive coccoid cells, rods, gram-negative anaerobes, and a low ratio of anaerobe/aerobes.[10,51] Failing implants show greater proportions of periodontal pathogens, including gram-negative anaerobe rods, fusiform bacteria, motile rods, and spirochetes.[52]

DIAGNOSIS OF PERI-IMPLANTITIS

Accurate and timely diagnosis of peri-implantitis is a clinical challenge and relies on accurate assessment of the status of peri-implant tissues.[23,53-55] Aspects commonly assessed are pain, probing depth, mobility, bleeding index and radiographic evaluation of bone loss.[23,54-57] Signs of peri-implant disease include bleeding or suppuration after probing, swelling, peri-implant pockets greater than 4 mm, bone loss or saucer-shaped radiolucency around the implant, implant mobility and pain.[58] The diagnosis of peri-implant mucositis is generally associated with the presence of exudate release, swelling and/or bleeding on probing but without loss of bone. Peri-implantitis exhibits crestal bone loss,[6,11,47,54,57] and moderate to advanced peri-implantitis is diagnosed by radiographs showing saucerization of bone loss around implant, loss of gingival attachment, probing depths greater than 4 mm, mobility of implant, bleeding and sup-

puration.[59,60] A scale developed by James and Misch for classifies peri-implant disease on the basis of clinical symptoms and radiographic appearance ranging from optimum conditions to absolute failure.[23] The major diagnostic parameters considered in the classification include absence of pain, probing depth, rigid fixation, bleeding index, and radiographic evaluation of bone loss. The classification into groupings is based on the following findings:

Group 1: In this group the implant causes no pain or tenderness upon palpitation or function, stable probing depth, no horizontal or vertical mobility under loads of 500 g, less than 1 mm bone loss in the preceding 3 years, no exudates, and no radiolucency.

Group 2: This group is indicative of mucositis, or inflammation without any bone loss. There may be presence or history of exudate, swelling and/or bleeding on probing but without crestal bone loss.

Group 3: This includes moderate peri-implantitis, in which patients exhibit some degree of bone loss, and chronic inflammatory reaction around the implant, but the implant remains stable in the bone.

Group 4: This group represents clinical failure, where implants cause pain upon palpitation or function, greater than 1 mm horizontal mobility (also presence of vertical mobility a possibility), uncontrolled exudate, and radiolucency upon radiographic examination.

Group 5: Here in this group there is absolute failure, which occurs when the implant is surgically removed or exfoliated by the body.[23]

MANAGEMENT OF PERI-IMPLANTITIS

Various therapeutic strategies are employed in the management of peri-implant diseases (peri-implant-mucositis & peri-implantitis) in order to prevent failure of implant treatment.[19,61-63] Implant removal is indicated only when peri-implantitis has led to loss of osseointegration with more than 60% loss of bone to implant contact along with mobility of implant.[19,23] The following literature discusses some of the available treatment strategies for the management of peri-implant disease.

Non-Surgical Mechanical Debridement

The first line of treatment of peri-implantitis is scaling and root planning, sometimes referred to as non-surgical debridement.[63] A metal or plastic instrument is used to physically scrape the subgingival surface of the implant around the affected areas. This is accompanied with oral hygiene instructions to make the patient follow a strict oral hygiene regimen. The purpose of scaling and root planning is to reduce the inflammation by mechanically disrupting the biofilm on the implant surface.[64] In some cases, scaling is also combined with chlorhexidine irrigation and/or topical application.[39] Concerns have been raised regarding scratching and roughening the implant-abutment assembly with scalers which may contribute to potential increased plaque accumulation.[65,66] Therefore, it is desired that scaling and surface decontamination processes should leave the surface smooth or to avoid further plaque accumulation.

Local Antimicrobial Delivery in Periodontitis and Peri-Implantitis

It has become standard practice in treatment of periodontitis to locally administer antibiotics to patients with moderate to severe disease progression.[67] To maintain a sustained level of antibiotic at the site of infection, controlled release devices such as chips, gels, polymeric fibers, or microcapsules have been investigated and developed.[68-72] Various antiseptics and antibiotics have been incorporated into these devices, including doxycycline, tetracycline, minocycline, chlorhexidine, and metronidazole.[72-77] These devices are intended to keep the concentration of antimicrobial agent elevated in the gingival crevicular fluid for an extended period before degrading or being removed. One approach is to use local delivery devices developed for treating periodontitis, and implement them in the management of peri-implantitis. However, Mombelli, et al. in their clinical study showed that it is difficult to advance a local delivery device to the bottom of a deep peri-implant pocket.[78] This indicates that simply using periodontal therapies to treat peri-implantitis may not be an adequate and ideal solution.

Surgical Debridement and Bone Grafting

When scaling, implant surface debridement and local anti-microbial therapies fail to cease the progression of peri-implantitis, surgical debridement may be necessary. This mainly involves the resection of affected tissues (granulation tissue), debridement, implant surface decontamination, followed by bone grafting, with or without the use of barrier membranes.[39] Barrier membranes are used to promote the osseointegration of the titanium surface, and provide a barrier for epithelial migration into the defect space.[21] These membranes can be natural or synthetic and can be fabricated using resorbable or non-resorbable materials.[21] Studies comparing the use of resorbable (polylactic acid) and non-resorbable membranes, such as expanded Polytetrafluoroethylene (ePTFE) have shown similar clinical efficacy for the two approaches.[79] In addition, Guided Tissue Regeneration (GTR) membranes, intended for periodontal bone regeneration and antimicrobial activity have been investigated. These GTR membranes are usually degradable and have been modified with tetracycline,[80] doxycycline,[81] chlorhexidine[82] and metronidazole.[83] Furthermore, Bone grafting materials are utilized for bone regeneration in combination with GTR membranes. There are four classes of bone-grafting materials based upon the mode of action:

i. Autografts: Autogenous bone (usually harvested from mandibular ramus and chin) is an organic material and forms bone

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by osteogenesis, osteoinduction, and osteoconduction.

ii. Allografts: Graft tissues such as demineralized freeze-dried bone are osteo-inductive and osteoconductive and may be cortical and/or trabecular in nature. Allograft is derived from humans and is harvested from an individual other than the one receiving the graft.

iii. Xenografts: Graft tissues harvested from animals, for instance bovine and porcine (Bio Oss). These usually contain mineral portion (hydroxyapatite) of the bone.

iv. Alloplasts: Synthetic grafts such as hydroxyapatite, tricalcium phosphate, dicalcium phosphates, bioactive glasses etc. may be synthetic or natural, vary in size, and are mainly osteoconductive. These can be further divided based upon the porosity of the product.[14,20,84]

Clinical studies have shown improvement in defect fill and probing depth when patients were treated with bone graft regardless of the use of resorbable membranes.[85] These materials have different properties and therefore their indications may vary. The use of the three classes of materials in diverse combinations depends upon the size and topography of the bony defect. Small defects or defects with four walls of host bone can be repaired with alloplasts alone or allografts in combination with alloplasts.[86,87] The mechanisms that provide a rationale for bone grafting are as follows:

Osteoconduction is a function of a bone graft that provides a tridimensional scaffold for ingrowth of host capillaries and osteoprogenitor cells.[88] The bone graft material serves as a scaffold for new bone growth and the osteoblasts from the margin of defect utilize the bone graft material as a framework upon which new bone formation occurs. Bone regeneration in early phases at grafted sites is dominated by active bone resorption and formation throughout the graft material. The latter phase is characterized by osteoconduction and a process known as creeping substitution.[89]

Osteoinduction involves stimulation of osteoprogenitor cells to differentiate into osteoblasts and then begins formation of new bone. The osteoblast precursors differentiate into mature osteoblasts under the influence of osteoinductors and synthesize new bone during the first weeks. Growth factors involved in bone formation act on fibroblast and osteoblast proliferation, extracellular matrix deposition, mesenchymal cell differentiation and vascular proliferation.[90] A bone graft material that is osteoinductive, not only serves as a scaffold for currently existing osteoblasts but will also trigger formation of new osteoblasts, promoting faster integration of the graft.

Osteogenesis occurs when vital osteoblasts originating from bone graft material contributes to the growth of new bone along with bone formation.[91] A requirement for bone regeneration is the presence or recruitment of osteoblast precursors and growth factors at sites of augmentation.

Osteopromotion involves the enhancement of osteoinduction process without possessing of the osteoinductive properties.[92] For example, enamel matrix derivative enhances the osteoinductive effect of demineralized freeze-dried bone allograft.[93]

CASE REPORT

A 49 year old male presented in the outpatient department complaining of swelling, bleeding on brushing and pain on chewing around the implant site in the anterior maxilla from 6 months (Figure 1).

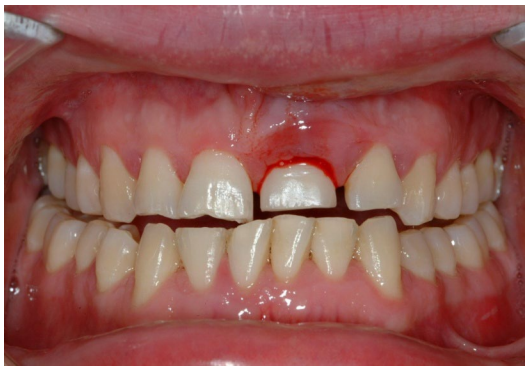

Figure 1: Pre-operative anterior view showing bleeding from the gingival margin of the affected implant.

Implant fixture was placed 4 years ago and was restored 3 months after surgical placement. Patient's oral hygiene was average with some plaque deposits on posterior teeth. The anterior tooth relation was in edge to edge incisor position. Clinical examination revealed gingival marginal bleeding, visible bone deficiency and mobile prosthetic component with displacement. The patient had extremely sensitive gingival tissues that bled instantly on probing and had a history of smoking. Patient was lacking in posterior stability due to moderate tooth wear on anterior teeth and over-eruption of mandibular anterior teeth. Excursive and protrusive guidance was on central and lateral incisors. Moderate to severe teeth attrition on anterior teeth was suggestive of heavy non-axial occlusal loading on the anterior teeth (Figure 2).

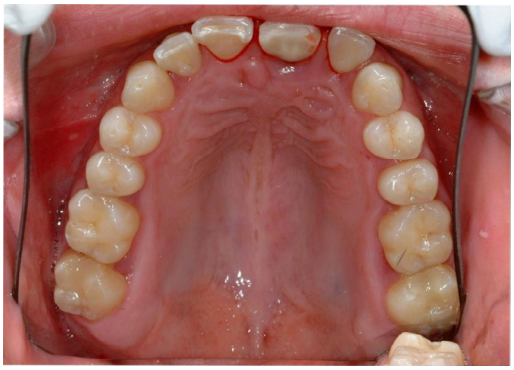

Figure 2: Pre-operative occlusal view.

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Implant was restored using a cement retained preformed standard abutment and cement retained crown. A periapical radiograph revealed significant bone defect around the marginal areas of the implant (Figure 3).

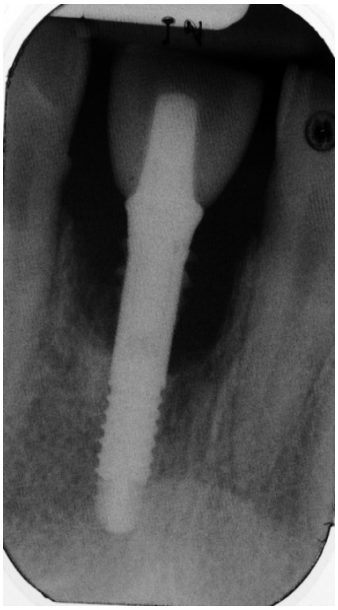

Figure 3: Pre-operative clinical radiograph showing bone resorption around the dental implant.

All of the above mentioned signs and symptoms, both clinical and radiographic were the classic indications of implant failure and peri-implantitis.

Treatment

After gathering all the relevant information, it was planned to undergo surgical debridement of the infected implant with peri-implantitis due to severe pocketing. Another goal of the surgical approach was to allow access for debridement and bone grafting. The abutment was removed and soft tissue flap was raised to expose the implant surface. Debridement (with removal of granulation tissue) of the implant surface and the defect was carried out and MinerOss Cortical & Cancellous (Biohorizons, USA) was placed in the defect followed by the placement of AlloDerm GBR (Biohorizons, USA). Soft tissue closure was carried out over a cover screw and post-operative instructions were given to the patient. Healing of the surgical wound was uneventful. At 8 weeks follow up, clinically soft tissue contours around the implant and the healing screw were well established. At 12 weeks follow up, radiographic appearance showed increased presence of bone around the implant fixture, at this stage impression was taken and the implant was loaded a week later with a standard implant abutment and cement retained crown. At 6 months follow up, peri-apical radiograph was taken to assess the implant and the surrounding tissues (Figure 4).

The implant fixture along with the prosthetic crown is seen in the desired position however, the bony defect had again started to occur. Clinically, signs of inflammation were visible again over the soft tissue surrounding the implanted tooth (Figure 5).

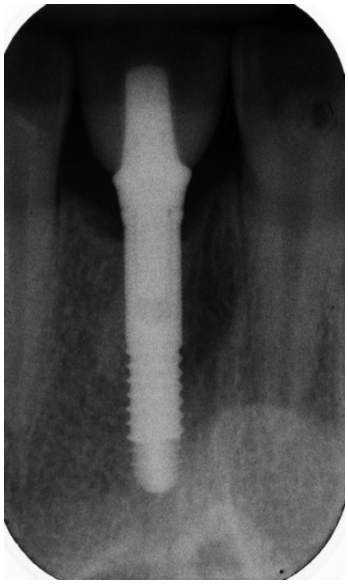

Figure 4: Post-operative clinical radiograph, taken 6 months after allograft placement showing higher bone levels in comparison with what was observed before treatment.

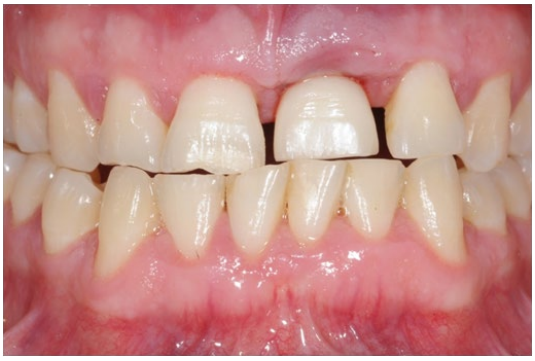

Figure 5: Post-operative anterior view, 6 months after treatment showing healthier soft tissue margins.

DISCUSSION

Endosseous dental implants have become quite significant in prosthodontics and restorative dentistry since the early 1970's.[94,95] Despite many advances in the techniques, materials and implant design, there is always the potential for clinical failure and hence it has been a significant concern both for the patient and the dentist. Dental implant failures occur occasionally, and clinicians may hesitate to perform a second implantation because of the uncertain prognosis.[96] This also underlines the necessity for a predictable treatment strategy for the maintenance and therapy of peri-implantitis. There is an acute lack of scientific guidelines for the management of peri-implantitis. As no agreed standard of care protocol for the treatment of peri-implantitis exists, it is reasonable to present a case report using principles previously reported to be efficacious in the treatment of periodontitis.[58]

Factors implicated in the etiology of the peri-implant infection include status of the tissue around implant, degree of roughness, external morphology and excessive mechanical load. Indicators of an implant failure include horizontal and vertical mobility, progressive bone loss, pain during percussion or function and infection.[97-99] While observing the clinical and the radiographic features of the patient, anterior attrition was evident with the history of heavy brushing, bruxism and smoking. According to the literature, the most common patient habits that adversely affect the dental implants are bruxism and smoking. Para functional habits (such as chewing ice and nibbling on hard objects) may cause premature implant failure.[32,100,101] In addition, the patient in this case report was also a smoker and several epidemiologic studies have shown the negative influence of smoking on periodontal status and an increased risk of developing periodontitis.[102-104] The relationship between smoking and implant failures has been evaluated in several retrospective and prospective clinical studies and there are reports that significantly greater percentage of implant failures occur in smokers than in non-smokers.[33,34,105] Therefore, it can be concluded that para functional activity in combination with smoking were major contributing factors in the development of peri-implantitis in the case presented in this report.

From the case reports available in literature, it can be concluded that treatment of peri-implantitis lesions with the combination of grafts and barrier membranes may lead to bone infill. However, the results of a comparative study by Khoury & Buchmann on treatment of peri-implantitis indicate that placement of barrier membranes in addition to bone grafting does not provide any adjunctive effects.[106] Unfortunately, not all peri-implantitis lesions are favorable to regeneration. For implants with thin facial and lingual walls, peri-implantitis typically does not produce a crater-form defect with four walls. In some of these cases, the defect will present as a complete loss of the surrounding bony walls leaving regeneration as an unpredictable treatment choice. Charalampakis, et al. evaluated the longevity and incidence of relapse of multiple different treatments on peri-implantitis lesions.[107] Over half of the cases evaluated relapsed and were not controlled. Patient habits and early disease development were associated with higher rates of relapse and surgical therapy with lower rates of relapse.[107] Long-term success of an implant depends on regular maintenance program. During maintenance phase, peri-implant tissue should be evaluated for inflammation. Patient education and relieving the possible risk factors need to be addressed to ensure longevity of the implant fixtures. All the treatment modalities in combination can result in a long-term good prognosis however; the treated cases must be watched closely as relapse is common.

CONCLUSIONS

In summary, development and management of peri-implantitis continues to be a challenge for dental practitioners and surgeons providing implant treatment. The microbial populations differ widely from patient to patient, and have the ability to change and develop over time which makes the treatment of peri-implantitis a difficult task. The use of bone allografts along with GTR in filling peri-implant defects is a pragmatic treatment option. However, there is lack of credible evidence suggesting that a specific treatment protocol or biomaterial is superior to others in treating peri-implant defects.

RECOMMENDATIONS

It is clear that several uncertainties still exist regarding management of peri-implantitis. Most of the studies reporting either open debridement with pocket reduction therapy or implant detoxification with the use of antibiotics for the treatment of peri-implantitis are case reports that are short-term and include a few cases only. However, long-term monitoring of consecutively treated cases in form of randomized controlled trials are further required. This will help in establishing predictable and stable improvements.

CONFLICTS OF INTEREST

The authors declare that they have no conflicts of interest.

CONSENT

Authors obtained written and informed consent from the patient for submission of this manuscript for this publication.

REFERENCES

1. Sheikh Z, Sima C, Glogauer M. Bone replacement materials and techniques used for achieving vertical alveolar bone augmentation. *Materials.* 2015; 8(6): 2953-2993. doi: 10.3390/ma8062953

2. Sheikh Z, Glogauer M. Successful ridge augmentation: The challenge of periodontal tissue engineering. *EC Dent Sci.* 2015; 2: 216-218.

3. Rosenberg ES, Cho SC, Elian N, Jalbout ZN, Froum S, Evian CI. A comparison of characteristics of implant failure and survival in periodontally compromised and periodontally healthy patients: A clinical report. *The Int J Oral Max Fac Imp.* 2004; 19(6): 873.

4. Snauwaert K, Duyck J, van Steenberghe D, QuirynenM, Naert I. Time dependent failure rate and marginal bone loss of implant supported prostheses: A 15-year follow-up study. *Clinical oral investigations.* 2000; 4(1): 13-20.

5. Esposito M, Hirsch J-M, Lekholm U, Thomsen P. Biological factors contributing to failures of osseointegrated oral implants, (II). Etiopathogenesis. *European journal of oral sciences.* 1998; 106(3): 721-764. doi: 10.1046/j.0909-8836..t01-6-.x

6. Klinge B, Hultin M, Berglundh T. Peri-implantitis. *Dental*

Clinics of North America. 2005; 49(3): 661-676.

7. Berglundh T, Persson L, Klinge B. A systematic review of the incidence of biological and technical complications in implant dentistry reported in prospective longitudinal studies of at least 5 years. *Journal of clinical periodontology.* 2002; 29(s3): 197-212. doi: 10.1034/j.1600-051X.29.s3.12.x

8. O'Mahony A, Spencer P. Osseointegrated implant failures. *Journal of the Irish Dental Association.* 1998. 45(2): 44-51.

9. Quirynen M, Vogels R, Peeters W. Dynamics of initial subgingival colonization of 'pristine'peri-implant pockets. *Clinical oral implants research.* 2006; 17(1): 25-37. doi: 10.1111/j.1600-0501.2005.01194.x

10. Quirynen M, De Soete M, Van Steenberghe D. Infectious risks for oral implants: A review of the literature. *Clinical oral implants research.* 2002; 13(1): 1-19. doi: 10.1034/j.1600-0501.2002.130101.x

11. Romeo E, Ghisolfi M, Carmagnola D. Peri-implant diseases: A systematic review of the literature. *Minerva stomatologica.* 2004; 53(5): 215-230.

12. Tonetti MS. Determination of the success and failure of root-form osseointegrated dental implants. *Advances in dental research.* 1999; 13(1): 173-180. doi: 10.1177/08959374990130010801

13. Piattelli A, Scaranoa A, Dalla Norab A, De Bonab G, Favero GA. Microscopical features in retrieved human Branemark implants: A report of 19 cases. *Biomaterials.* 1998; 19(7): 643-649. doi: 10.1016/S0142-9612(97)00158-0

14. Quirynen M, et al. The intra-oral translocation of periodontopathogens jeopardises the outcome of periodontal therapy. *Journal of Clinical Periodontology.* 2001; 28(6): 499-507. doi: 10.1034/j.1600-051x.2001.028006499.x

15. Esposito M, Hirsch J, Lekholm U, Thomsen P. Differential diagnosis and treatment strategies for biologic complications and failing oral implants: A review of the literature. *International Journal of Oral and Maxillofacial Implants.* 1999; 14(4): 473-490.

16. Teughels W, Van Assche N, Sliepen I, Quirynen M. Effect of material characteristics and/or surface topography on biofilm development. *Clinical oral implants research.* 2006; 17(S2): 68-81. doi: 10.1111/j.1600-0501.2006.01353.x

17. Quirynen M, Teughels W. Microbiologically compromised patients and impact on oral implants. *Periodontology* 2000. 2003; 33(1): 119-128. doi: 10.1046/j.0906-6713.2003.03310.x

18. Tonetti MS. Risk factors for osseodisintegration. *Periodontology.* 2000; 1998. 17(1): 55-62. doi: 10.1111/j.1600-0757.1998.tb00123.x

19. Lang NP, Lindhe J. Clinical periodontology and implant dentistry. New York, USA: John Wiley & Sons; 2015

20. Sheikh ZA, Javaid A, Abdallah MA, Bone MN. *Replacement Graft Materials in Dentistry*. In: Khurshid SZ, ed. Dental Biomaterials (Principle and its Application). Karachi, Pakistan: Paramount Publishing Enterprise; 2013.

21. Zeeshan Sheikh MA. Hamdan N, Javaid MA, Khurshid Z. Barrier membranes for tissue regeneration and bone augmentation techniques in dentistry in Handbook of Oral Biomaterials. In: Matilinna KP, ed. Singapore: Pan Stanford Publishing; 2014.

22. Tamimi F, Sheikh Z, Barralet J. Dicalcium phosphate cements: brushite and monetite. *Acta Biomater*. 2012; 8(2): 474-87.

23. Misch CE. Contemporary Implant Dentistry. Oxford, UK: Elsevier Health Sciences; 2007.

24. Mombelli A, Lang N. Antimicrobial treatment of peri-implant infections. *Clinical oral implants research.* 1992; 3(4): 162-168.

25. Tonetti MS, Schmid J. Pathogenesis of implant failures. *Periodontology.* 2000. 1994; 4(1): 127-138. doi: 10.1111/j.1600-0757.1994.tb00013.x

26. Misch CE. Contemporary implant dentistry. *Implant Dentistry*. 1999; 8(1): 90.

27. Rokn AR, Sajedinejad N, Yousefyfakhr H, Badri S. An unusual bone loss around implants. *Journal of Dentistry (Tehran, Iran)*. 2013; 10(4): 388.

28. Roller MB, Li Y, Yuan JJ. Implantable medical devices and methods for making same. 2009; *Google Patents.*

29. Costerton J, Montanaro L, Arciola C. Biofilm in implant infections: its production and regulation. *The International journal of artificial organs*. 2005; 28(11): 1062-1068.

30. Ferreira S, Silva GL, Cortelli JR, Costa JE, Costa FO. Prevalence and risk variables for peri-implant disease in Brazilian subjects. *Journal of Clinical Periodontology*. 2006; 33(12): 929-935.

31. Ellegaard B, Baelum V, Karring T. Implant therapy in periodontally compromised patients. *Clinical Oral Implants Research.* 1997; 8(3): 180-188. doi: 10.1034/j.1600-0501.1997.080304.x

32. Karoussis IK, Salvi GE, Heitz-Mayfield LJ, Brägger U,

Hämmerle CH, Lang NP. Long-term implant prognosis in patients with and without a history of chronic periodontitis: A 10 year prospective cohort study of the ITI® Dental Implant System. *Clinical Oral Implants Research.* 2003; 14(3): 329-339. doi: 10.1034/j.1600-0501.000.00934.x

33. De Bruyn H, Collaert B. The effect of smoking on early implant failure. *Clinical oral implants research.* 1994; 5(4): 260-264. doi: 10.1034/j.1600-0501.1994.050410.x

34. Bain CA, Moy PK. The association between the failure of dental implants and cigarette smoking. *The International journal of oral & maxillofacial implants.* 1992; 8(6): 609-615.

35. Bain CA. Smoking and implant failure--benefits of a smoking cessation protocol. *The International journal of oral & maxillofacial implants.* 1995; 11(6): 756-759.

36. Quirynen M, Bollen C. The influence of surface roughness and surfacefree energy on supra and subgingival plaque formation in man. *Journal of clinical periodontology.* 1995; 22(1): 1-14.

37. Weyant RJ. Characteristics associated with the loss and peri-implant tissue health of endosseous dental implants. *The International journal of oral & maxillofacial implants.* 1993; 9(1): 95-102.

38. Piattelli A, Cosci F, Scarano A, Trisi P. Localized chronic suppurative bone infection as a sequel of peri-implantitis in a hydroxyapatite-coated dental implant. *Biomaterials*. 1995; 16(12): 917-920. doi: 10.1016/0142-9612(95)93116-U

39. Norowski PA, Bumgardner JD. Biomaterial and antibiotic strategies for periimplantitis: a review. *Journal of Biomedical Materials Research Part B: Applied Biomaterials.* 2009; 88(2): 530-543. doi: 10.1002/jbm.b.31152

40. Silverstein LH, Kurtzman D, Garnick JJ, Schuster GS, Steflik DE, Moskowitz ME. The microbiota of the peri-implant region in health and disease. *Implant dentistry.* 1994; 3(3): 170-175.

41. Heydenrijk K, Meijer HJ, van der Reijden WA, Raghoebar GM, Vissink A, Stegenga B. Microbiota around root-form endosseous implants: a review of the literature. *The International journal of oral & maxillofacial implants.* 2001; 17(6): 829-838.

42. Van Houte J. Role of micro-organisms in caries etiology. *Journal of dental research.* 1994; 73(3): 672-681. doi: 10.1177/00220345940730031301

43. Karbach J, Callaway A, Kwon YD, d'Hoedt B, Al-Nawas B. Comparison of five parameters as risk factors for peri-mucositis. *The International journal of oral & maxillofacial implants.* 2008; 24(3): 491-496.

44. Takanashi K, Kishi M, Okuda K, Ishihara K. Colonization by Porphyromonas gingivalis and Prevotella intermedia from teeth to osseointegrated implant regions. *The Bulletin of Tokyo Dental College.* 2004; 45(2): 77-85. doi: 10.2209/tdcpublication.45.77

45. Heuer W, Elter C, Demling A, et al. Analysis of early biofilm formation on oral implants in man. *Journal of oral rehabilitation.* 2007; 34(5): 377-382.

46. Broggini N, , McManus LM, Hermann JS, et al. Peri-implant inflammation defined by the implant-abutment interface. *Journal of Dental Research.* 2006; 85(5): 473-478. doi: 10.1177/154405910608500515

47. Meffert R. Periodontitis vs. peri-implantitis: the same disease? The same treatment? *Critical Reviews in Oral Biology & Medicine.* 1996; 7(3): 278-291. doi: 10.1177/10454411960070030501

48. Listgarten MA. Microorganisms and dental implants. *Journal of periodontology,* 1999; 70(2): 220-222.

49. Mombelli A. Microbiology of the dental implant. *Advances in dental research,* 1993; 7(2): 202-206.

50. Sbordone L, Bortolaia C. Oral microbial biofilms and plaque-related diseases: microbial communities and their role in the shift from oral health to disease. *Clinical oral investigations,* 2003; 7(4): 181-188. doi: 10.1007/s00784-003-0236-1

51. George K, Zafiropoulos GGK, Murat Y, Hubertus S, Nisengard RJ. Clinical and microbiological status of osseointegrated implants. *Journal of periodontology,* 1994; 65(8): 766-770. doi: 10.1902/jop.1994.65.8.766

52. Mombelli A, an Oosten MA, Schurch E Jr, Land NP. The microbiota associated with successful or failing osseointegrated titanium implants. *Oral microbiology and immunology,* 1987; 2(4): 145-151.

53. Wingrove SS. Peri-implant therapy for the dental hygienist: clinical guide to maintenance and disease complications. 2013: John Wiley & Sons.

54. Mombelli A, Lang NP. The diagnosis and treatment of peri-implantitis. *Periodontology 2000.* 1998; 17(1): 63-76. doi: 10.1111/j.1600-0757.1998.tb00124.x

55. Mombelli A. Etiology, diagnosis, and treatment considerations in peri-implantitis. *Current opinion in Periodontology.* 1996; 4: 127-136.

56. RoosJansåker AM, Almhöjd US, Jansson H. Treatment of peri-implantitis: clinical outcome of chloramine as an adjunctive to non-surgical therapy, a randomized clinical trial. *Clinical oral implants research.* 2015. doi: 10.1111/clr.12612

57. Meffert RM, Langer B, Fritz ME. Dental implants: a review. *Journal of periodontology.* 1992; 63(11): 859-870.

58. Jepsen S, Berglundh T, Genco R, et al. Primary prevention of peri-implantitis: Managing peri-implant mucositis. *Journal of clinical periodontology.* 2015; 42(S16): S152-S157. doi: 10.1111/jcpe.12369

59. Dewan SK, Arora A, Sehgal M, Khullar A. Implant failures: a broader perspective. *Journal of Dental Implants.* 2015; 5(1): 53-59.

60. Van Steenberghe D, Naert I, Jacobs R, Quirynen M. Influence of inflammatory reactions *vs*. occlusal loading on peri-implant marginal bone level. *Advances in dental research.* 1999. 13(1): 130-135. doi: 10.1177/08959374990130010201

61. Roos-Jansåker AM, Renvert S, Egelberg J. Treatment of peri-implant infections: a literature review. *Journal of clinical periodontology.* 2003; 30(6): 467-485.

62. Lang NP, Mombelli A, Tonetti MS, Brägger U, Hämmerle CH. Clinical trials on therapies for peri-implant infections. *Annals of Periodontology.* 1997. 2(1): 343-356.

63. Renvert S, Polyzois IN. Clinical approaches to treat peri-implant mucositis and peri implantitis. *Periodontology 2000.* 2015; 68(1): 369-404.

64. Pihlstrom BL, Michalowicz BS, Johnson NW. Periodontal diseases. *The Lancet.* 2005; 366(9499): 1809-1820.

65. Matarasso S, Quaremba G, Coraggio F, Vaia E, Cafiero C, Lang NP. Maintenance of implants: an in vitro study of titanium implant surface modifications subsequent to the application of different prophylaxis procedures. *Clinical oral implants research.* 1996; 7(1): 64-72. doi: 10.1034/j.1600-0501.1996.070108.x

66. McCollum J, O'Neal RB, Brennan WA, Van Dyke TE, Horner JA. The effect of titanium implant abutment surface irregularities on plaque accumulation in vivo. *Journal of periodontology.* 1992; 63(10): 802-805. doi: 10.1902/jop.1992.63.10.802

67. Schenk G, Flemmig TF, Betz T, Reuther J, Klaiber B. Controlled local delivery of tetracycline HCl in the treatment of periimplant mucosal hyperplasia and mucositis: A controlled case series. *Clinical oral implants research.* 1997; 8(5): 427-433.

68. Garrett S, Adams DF, Bogle G, et al. The effect of locally delivered controlled-release doxycycline or scaling and root planing on periodontal maintenance patients over 9 months. *Journal of periodontology.* 2000; 71(1): 22-30. doi: 10.1902/jop.2000.71.1.22

69. Pedrazzoli V, Kilian M, Karring T. Comparative clinical and microbiological effects of topical subgingival application of metronidazole 25% dental gel and scaling in the treatment of adult periodontitis. *Journal of clinical periodontology.* 1992; 19(9): 715-722. doi: 10.1111/j.1600-051X.1992.tb02534.x

70. Hill M, Moore R. Locally acting oral chemotherapeutic agents. Periodontics. Medicine, surgery, and implants. In: Rose L, Mealey B, eds. St. Louis, MO, USA: Elsevier Mosby; 2004: 276-287.

71. Mombelli A, et al. Treatment of peri-implantitis by local delivery of tetracycline. *Clinical Oral Implants Research.* 2001. 12(4): 287-294.

72. Jeffcoat MK, Bray KS, Ciancio SG, et al. Adjunctive use of a subgingival controlled-release chlorhexidine chip reduces probing depth and improves attachment level compared with scaling and root planing alone. *Journal of periodontology.* 1998; 69(9): 989-997. doi: 10.1902/jop.1998.69.9.989

73. Salvi GE, Persson GR, Heitz-Mayfield LJ, Frei M, Lang NP. Adjunctive local antibiotic therapy in the treatment of peri-implantitis II: Clinical and radiographic outcomes. *Clinical oral implants research*. 2007; 18(3): 281-285. doi: 10.1111/j.1600-0501.2007.01377.x

74. Killoy WJ. Chemical treatment of periodontitis: local delivery of antimicrobials. *International dental journal.* 1998; 48(S3): 305-315.

75. Rose LF. Periodontics: medicine, surgery, and implants. 2004: Mosby Incorporated.

76. Mombelli A, Lehmann B, Tonetti M, Lang NP. Clinical response to local delivery of tetracycline in relation to overall and local periodontal conditions. *Journal of clinical periodontology*. 1997; 24(7): 470-477. doi: 10.1111/j.1600-051X.1997.tb00214.x

77. Fourmousis I, Tonetti MS, Mombelli A, Lehmann B, Lang NP, Brägger U. Evaluation of tetracycline fiber therapy with digital image analysis. *Journal of clinical periodontology.* 1998; 25(9): 737-745. doi: 10.1111/j.1600-051X.1998.tb02515.x

78. Mombelli A. Microbiology and antimicrobial therapy of peri-implantitis. *Periodontology 2000.* 2002; 28(1): 177-189. doi: 10.1034/j.1600-0757.2002.280107.x

79. Zybutz MD, Laurell L, Rapoport DA, Persson GR. Treatment of intrabony defects with resorbable materials, non-resorbable materials and flap debridement. *Journal of clinical periodontology,* 2000; 27(3): 169-178. doi: 10.1034/j.1600-051x.2000.027003169.x

80. Park YJ, Lee YM, Park SN, et al. Enhanced guided bone regeneration by controlled tetracycline release from poly (L lactide) barrier membranes. *Jour-*

nal of biomedical materials research. 2000; 51(3): 391-397. doi: 10.1002/1097-4636(20000905)51:3<391::AID-JBM13>3.0.CO;2-9

81. Chang CY, Yamada S. Evaluation of the regenerative effect of a 25% doxycycline-loaded biodegradable membrane for guided tissue regeneration. *J Periodontol*. 2000; 71(7): 1086-1093. doi: 10.1902/jop.2000.71.7.1086

82. Chen YT, Hung SL, Lin LW, Chi LY, Ling LJ. Attachment of periodontal ligament cells to chlorhexidine-loaded guided tissue regeneration membranes. *J Periodontol.* 2003; 74(11): 1652-1659. doi: 10.1902/jop.2003.74.11.1652

83. Kurtis B, Unsal B, Cetiner D, et al. Effect of polylactide/glycolide (PLGA) membranes loaded with metronidazole on periodontal regeneration following guided tissue regeneration in dogs. *J Periodontol.* 2002; 73(7): 694-700. doi: 10.1902/jop.2002.73.7.694

84. Sheikh Z, Zhang YL, Grover L, Merle GE, Tamimi F, Barralet J. In vitro degradation and in vivo resorption of dicalcium phosphate cement based grafts. *Acta biomaterialia.* 2015; 26: 338-346. doi: 10.1016/j.actbio.2015.08.031

85. Roos Jansåker AM, Renvert H, Lindahl C, Renvert S. Surgical treatment of peri-implantitis using a bone substitute with or without a resorbable membrane: A prospective cohort study. *Journal of clinical periodontology.* 2007; 34(7): 625-632. doi: 10.1111/j.1600-051X.2007.01102.x

86. Laurencin C, Khan Y, El-Amin SF. Bone graft substitutes. *Expert review of medical devices.* 2006; 3(1): 49-57. doi: 10.1586/17434440.3.1.49

87. Giannoudis PV, Dinopoulos H, Tsiridis E. Bone substitutes: an update. *Injury.* 2005; 36(3): S20-S27.

88. Goldberg VM. Natural history of autografts and allografts. *Bone implant grafting*. 1992; 9-12. doi: 10.1007/978-1-4471-1934-0_2

89. Sheikh Z, Javaid MA, Hamdan N, Hashmi R. Bone regeneration using bone morphogenetic proteins and various biomaterial carriers. *Materials.* 2015; 8(4): 1778-1816. doi: 10.3390/ma8041778

90. Albrektsson T, Johansson C. Osteoinduction, osteoconduction and osseointegration. *European Spine Journal.* 2001; 10(2): S96-S101. doi: 10.1007/s005860100282

91. Buckwalter J, Glimcher MJ, Cooper RR, Recker R. Bone biology. II: formation, form, modeling, remodeling, and regulation of cell function. *J Bone Joint Surg Am*. 1995; 77(8): 1276-1289.

92. Linde A, Alberius P, Dahlin C, Bjurstam K, Sundin Y. Osteopromotion: A Soft-Tissue Exclusion Principle Using a Membrane for Bone Healing and Bone Neogenesis. *J Periodontol.* 1993. 64(11s): 1116-1128. doi: 10.1902/jop.1993.64.11s.1116

93. Schwartz Z, Mellonig JT, Carnes DL Jr, et al. Ability of commercial demineralized freeze-dried bone allograft to induce new bone formation. *J Periodontol.* 1996; 67(9): 918-926. doi: 10.1902/jop.1996.67.9.918

94. Taylor TD, Agar JR. Twenty years of progress in implant prosthodontics. *The Journal of prosthetic dentistry.* 2002; 88(1): 89-95. doi: 10.1067/mpr.2002.126818

95. Smith DE, Zarb GA. Criteria for success of osseointegrated endosseous implants. *The Journal of prosthetic dentistry.* 1989; 62(5): 567-572.

96. KimYK, Park JY, Kim SG, Lee HJ. Prognosis of the implants replaced after removal of failed dental implants. *Oral Surgery, Oral Medicine, Oral Pathology, Oral Radiology, and Endodontology.* 2010; 110(3): 281-286. doi: 10.1016/j.tripleo.2010.01.031

97. Al-Sabbagh M. Complications in implant dentistry. *Dental Clinics.* 2015; 59(1): 13-15.

98. El Askary AS, Meffert RM, Griffin T. Why do dental implants fail? Part I. *Implant dentistry.* 1999; 8(2): 173-185.

99. Misch CE. Dental Implant Prosthetics. Oxford, UK: Elsevier Health Sciences; 2014.

100. Duyck J, Naert I. Failure of oral implants: aetiology, symptoms and influencing factors. *Clinical oral investigations.* 1998; 2(3): 102-114.

101. Polizzi G, Grunder U, Goené R, et al. Immediate and delayed implant placement into extraction sockets: A 5 year report. *Clin Implant Dent Relat Res.* 2000; 2(2): 93-99.

102. Bergström J, Eliasson S, Preber H. Cigarette smoking and periodontal bone loss. *J Periodontol.* 1991; 62(4): 242-246. doi: 10.1902/jop.1991.62.4.242

103. Norderyd O, Hugoson A, Grusovin G. Risk of severe periodontal disease in a Swedish adult population. *J Clin Periodontol.* 1999; 26(9): 608-615. doi: 10.1111/j.1600-051X.1998.tb02408.x

104. Papapanou PN. Periodontal diseases: epidemiology. *Ann Periodontol.* 1996; 1(1): 1-36.

105. Gorman M, Lambert PM, Morris HF, Ochi S, Winkler S. The effect of smoking on implant survival at second-stage surgery: DICRG interim report no. 5. *Implant dentistry*. 1994; 3(3): 165.

ISSN 2377-1623 Open Journal http://dx.doi.org/10.17140/DOJ-2-117

106. Khoury F, Buchmann R. Surgical therapy of peri-implant disease: a 3-year follow-up study of cases treated with 3 different techniques of bone regeneration. *J Periodontol.* 2001; 72(11): 1498-1508. doi: 10.1902/jop.2001.72.11.1498

107. Charalampakis G, Rabe P, Leonhardt A, Dahlén G. A followup study of peri-implantitis cases after treatment. *J Clin Periodontol.* 2011; 38(9): 864-871. doi: 10.1111/j.1600-051X.2011.01759.x