Chapter

Peri-Implantitis Revisited

Amer Shatta and Sukumaran Anil

Abstract

Dental implants have become a well-accepted treatment option for patients with partial or complete edentulism. The long-term success of the endosseous dental implant depends not only on osseointegration, but on the healthy soft tissue interface that surrounds the implant. Peri-implantitis is defined as an inflammatory process affecting the supporting hard and soft tissue around an implant in function, leading to loss of supporting bone. Peri-implant mucositis has been defined as a reversible inflammatory reaction in the peri-implant mucosa surrounding an osseointegrated dental implant. Peri-implant mucositis is assumed to precede peri-implantitis. Data indicate that patients diagnosed with peri-implant mucositis may develop peri-implantitis, especially in the absence of regular maintenance care. However, the features or conditions characterizing the progression from peri-implant mucositis to peri-implantitis in susceptible patients have not been identified. The most common etiological factors associated with the development of peri-implantitis are the presence of bacterial plaque and host response. The risk factors associated with peri-implant bone loss include smoking combined with IL-1 genotype polymorphism, a history of periodontitis, poor compliance with treatment and oral hygiene practices, the presence of systemic diseases affecting healing, cement left behind following cementation of the crowns, lack of keratinized gingiva, and previous history of implant failure There is strong evidence that there is an increased risk of developing peri-implantitis in patients who have a history of severe periodontitis, poor plaque control, and no regular maintenance care after implant therapy. Management of peri-implantitis generally works on the assumption that there is a primary microbial etiology. Furthermore, it is assumed that micro-organisms and/or their by-products lead to infection of the surrounding tissues and subsequent destruction of the alveolar bone surrounding an implant. A combination of surgical, open debridement, and antimicrobial treatment has been advocated for the treatment of peri-implantitis. Surgical intervention is required once a patient has bleeding on probing, greater than 5 mm of probing depth, and severe bone loss beyond that expected with remodeling. Access flaps require full-thickness elevation of the mucoperiosteum, facilitating debridement and decontamination of the implant surface *via* hand instruments, ultrasonic tips, or lasers. When necessary, surgical procedures may be used in conjunction with detoxification of the implant surface by mechanical devices, such as high-pressure air powder abrasion or laser.

Keywords: dental implant, peri-implant disease, peri-implant mucositis, peri-implantitis, periodontitis, risk factors

1. Introduction

Dental implants have become a well-accepted treatment option for patients with partial or complete edentulism. The long-term success of the endosseous dental implant depends not only on osseointegration, but on the healthy soft tissue interface that surrounds the implant [1]. Dental implants are susceptible to disease, and they might develop inflammatory reactions, which might lead to peri-implant mucositis and/or peri-implantitis.

Peri-implant disease progresses quietly without pain and often starts with marginal bone loss. The factors responsible can be broadly classified as biological factors and biomechanical factors. The biological factors include progressive bone loss, bacterial infections, and microbial plaque [2]. Biological complications are grouped as early biological failures and late implant failures. The early failures are applied to inappropriate aseptic measures of the surgical implant [3], and late complications are typically infections caused by peri-implantitis and bacterial plaque. Peri-implantitis due to biomechanical factors are either prosthesis-related factors such as occlusal overload, residual cement, inadequate prosthetic placement, or inappropriate abutment angle and bruxism [4].

2. Definitions

2.1 Peri-implant mucositis

Peri-implant mucositis is defined as inflammation of the peri-implant mucosa around an osseointegrated implant without loss of the supporting bone. Clinical signs of peri-implant inflammation are bleeding and/or suppuration on probing, with or without increased probing depths [5, 6].

2.2 Peri-implantitis

Peri-implantitis is defined as a pathological condition characterized by inflammation in the peri-implant mucosa/connective tissue and progressive loss of the supporting bone around a dental implant. Clinical signs of peri-implantitis are bleeding and/or suppuration on probing, increasing probing depths, and/or recession of the mucosal margin, in addition to radiographic bone loss compared to previous examinations. When a previous radiograph is not available, the following is indicative for the diagnosis of peri-implantitis: bone loss >3 mm in combination with bleeding on probing and pocket depth > 6 mm [5].

3. Diagnosis of peri-implantitis

The advanced case of peri-implantitis can be identifiable with the evidence of radiographic bone loss, mobility, and clinical signs of infection. The challenge is to diagnose the early stage of peri-implantitis that will aid in the prevention of further bone resorption and subsequent loss of the implant. Diagnosing peri-implant diseases using periodontal probing and radiographs may be inaccurate and only provides a historical record of past disease rather than current disease activity (**Figure 1**).

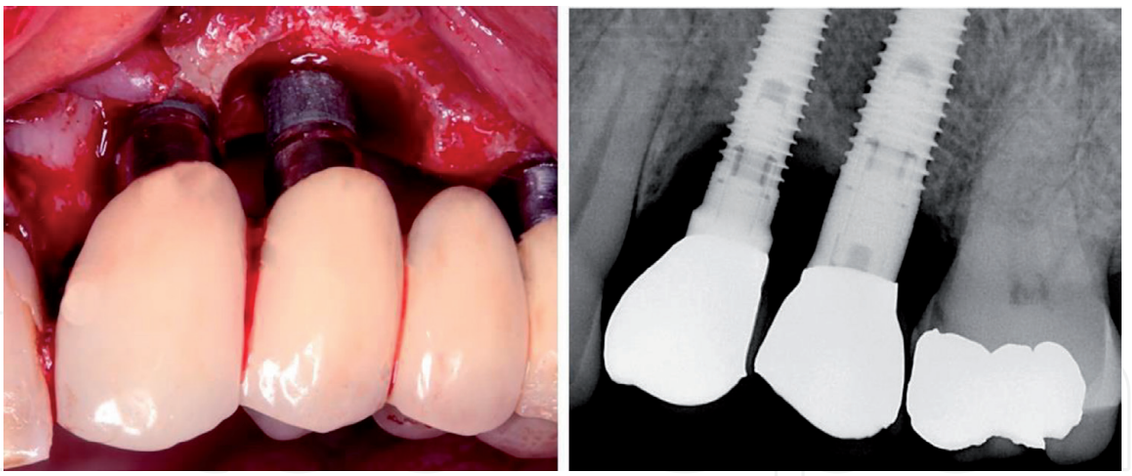

Figure 1.
The clinical and radiographic appearance of peri-implantitis.

Some of the clinical parameters used for the diagnosis are as follows [7]:

- Vertical destruction of the crestal bone,
- Formation of a peri-implant pocket >4 mm,
- Bleeding or suppuration after gently probing,
- Tissue redness and swelling,
- Mobility.

Developing biomarker technologies may offer possibilities in the diagnostic application. Although more research is needed, the assessment of proinflammatory cytokines (IL-1β, TNFα, MMP-8) in the peri-implant crevicular fluid may be of value to diagnose peri-implantitis and peri-implant mucositis but are, at this time, inappropriate to predict peri-implantitis because of the limited evidence of controlled longitudinal clinical trials. MMP-8 is a promising biomarker as an early signal of peri-implant inflammation [8]. Commercially available chair-side diagnostic tests for MMP-8 to detect peri-implant diseases are promising. Elevated levels of MMP-8 in peri-implant crevicular fluid (PICF) are associated with peri-implant inflammation, while low MMP-8 levels (<20 ng/mL) indicate healthy peri-implant tissues. Pathologically elevated levels of MMP-8 (>20 ng/mL) can be detected by a quantitative MMP-8 chair-side device, ImplantSafe® [9].

4. Classification peri-implantitis

Currently, there is no standard classification system to classify the parameters and the severity of the peri-implant disease. Froum and Rosen [10] proposed a classification for peri-implant disease based on the disease severity. This classification includes three clinical stages:

Early: Pocket depth (PD) ≥ 4 mm (bleeding and/or suppuration on probing) Bone loss <25% of the implant length.

Moderate: PD ≥ 6 mm (bleeding and/or suppuration on probing) bone loss 25–50% of the implant length.

Advanced: PD ≥ 8 mm (bleeding and/or suppuration on probing) bone loss >50% of the implant length.

Bleeding on probing should be noted on two or more aspects of the implant, and bone loss is measured on the radiographs from the time of prosthetic loading to the current time. If the radiograph at prosthetic loading is not available, the earliest available radiograph following loading should be used [11].

5. Pattern of bone loss in peri-implantitis

The pattern of bone loss in peri-implantitis is classified into vertical, horizontal, and combined bone loss. The most common pattern of bone loss is vertical (65%) and then horizontal (22%), and the least common pattern is combined (13%) [11].

6. Prevalence of peri-implantitis

The prevalence of peri-implant mucositis and peri-implantitis has ranged from 19 to 65% and 1 to 47%, respectively [12, 13]. A systematic review revealed that the frequency of peri-implant mucositis was 63.4% on the patient level and 30.7% on the implant level. The peri-implantitis prevalence was 18.8 and 9.6%. In smokers, the frequency of peri-implantitis increased to 36.3% [11]. The prevalence of peri-implant mucositis at the patient level varied between 1.1 and 80% [14–19]. The prevalence of peri-implantitis at the patient level ranged from 1.4 to 53.3% [14, 15, 17–26].

7. Etiology of peri-implantitis

Peri-implantitis is a result of biofilm-induced inflammation in the soft tissue that subsequently triggers a host response, with possible tissue degradation [27]. Peri-implantits inflammation is initiated by the accumulated bacterial biofilm. The development of disease was initially studied in an experimental gingivitis model in animals (dogs) and humans, and a cause-effect relationship between *de novo* plaque formation and peri-implant mucositis was observed [28, 29].

Histopathological, the early biofilm-induced inflammatory host response in mucositis is comparable to that in gingivitis, but the lesion of the inflammatory connective tissue (ICT) is larger and extends apically to the junctional epithelium. The established biofilm results in a more pronounced host response, and the extension of the ICT lesion is even larger in size than that in gingivitis, with the increased amounts of inflammatory cells in peri-implant mucositis [30]. The inflammation is reversible after biofilm removal, and no difference between implant systems has been observed [29, 31, 32]. Peri-implantitis lesions investigated in experimental ligature-induced peri-implantitis in a dog model presented more aggressive tissue degradation at the implant site than teeth with periodontitis. A larger inflammatory infiltrate extending close to the crestal bone and more bone-resorbing osteoclasts were observed at the implant site. Spontaneous progression after ligature removal varied with different implant surfaces [33, 34]. Peri-implant inflammation develops when microbes activate the host's innate and adaptive immune responses. Several cell types, such as epithelial cells, fibroblasts, stromal cells, endothelial cells, and osteoblasts, release pro-inflammatory mediators, such as cytokines and

chemokines, to recruit leukocytes. Leukocytes are recruited from blood vessels and tissues. Human biopsies revealed that the proportion of vascular structures was smaller within the peri-implant ICT lesion and greater lateral to the peri-implant ICT than reported for periodontitis lesions. Neutrophil granulocytes (polymorphonuclear neutrophils [PMNs]) and monocytes/macrophages are prevalent close to the sulcus epithelium in the peri-vascular area and the center of the ICT. Although the ICT lesion is dominated by T and B lymphocytes and plasma cells, the inflammatory lesion has a more acute character in peri-implantitis than in chronic periodontitis, with a larger proportion of PMNs and macrophages [35–37].

8. Risk factors associated with peri-implantitis

8.1 Poor plaque control and lack of regular supportive therapy

Poor plaque control and a lack of regular supportive therapy constitute the risk factors for developing peri-implantitis. A 5-year follow-up revealed a lower incidence of peri-implantitis with regular supportive care [20]. A 10-year follow-up study also revealed that patients on a regular maintenance program had less chances of developing peri-implantitis [38].

8.2 History of periodontitis

Patients who have lost teeth from periodontitis are treated with implants, and these patients may be more at risk of peri-implantitis disease. There is strong evidence from longitudinal and cross-sectional studies that a history of periodontitis constitutes a risk factor for peri-implantitis. Systematic reviews have indicated that subjects with a history of periodontitis are at greater risk of peri-implant disease. Long-term follow-up studies also revealed a correlation between peri-implantitis development with periodontitis [38–40].

8.3 Genetic traits

Genetic trait studies are scarce, and the overall evidence is limited and inconclusive. The most thoroughly investigated genetic factor is interleukin (IL)-1 composite gene polymorphism [41]. The genetic traits can influence susceptibility to peri-implantitis development in periodontitis patients, even if the inflammatory condition is under control at the time of implant placement. IL-1RN gene polymorphism was proposed as a risk factor for peri-implantitis [42]. The IL-1 genotype in combination with smoking was observed to affect implant failure [43]. The vascular endothelial growth factor (VEGF) may play a protective role in marginal bone loss, that is, peri-implantitis [36].

8.4 Diabetes mellitus

Based on the available data, no association was found between diabetes and peri-implantitis. Although the role of distinct physiological mediators in pathogenesis is not fully understood, evidence suggests that pro-inflammatory gene expression in peri-implantitis regions is affected by glycemic control [44]. Patients with diabetes mellitus are more prone to peri-implantitis than non-diabetic subjects, and the poor metabolic control has been shown to provide a more favorable environment for infection and loss of implants [45]. Controlling the blood sugar level is critical in increasing the implant success rate in diabetic patients [46].

8.5 Smoking

Smoking has a detrimental effect on tissue healing. Nicotine can reduce the nutrition to the tissues as a result of its vasoconstrictive effect on the blood vessels during the early osseointegration phase. Based on the available studies, smoking can be considered as a greatest identifiable risk factor for peri-implantitis. The extent of osseointegration as well as the plaque accumulation around dental implants was compromised among csmokers. A 10-year cohort study reported that peri-implantitis developed for 28% of all implants in smokers, while the corresponding incidence was 6% of all implants in non-smokers [39]. Several cross-sectional studies also showed a higher prevalence of peri-implantitis among smokers [15, 47, 48]. A systematic review of prospective and retrospective studies indicated an enhanced risk of biological complications among smokers; similarly, a meta-analysis indicated an enhanced risk of implant failure among smokers [49]. Studies indicate smoking as the greatest identifiable and most often cited risk.

8.6 Keratinized mucosa

Compared to sites with a keratinized mucosa of greater than 2 mm, sites with a keratinized mucosa of less than 2 mm are associated with plaque accumulation followed by peri-implant inflammation in the soft tissue and radiographic bone loss [50]. The evidence is limited and controversial that the absence of a keratinized mucosa is a risk factor for peri-implantitis, but this factor may negatively affect self-performed oral hygiene (**Figure 2**) [50].

8.7 Excess cement and over-contoured supra-structures

Potential risk indicators that are indirectly related to plaque accumulation have been proposed; for example, constructions with excess cement may result in a higher prevalence of peri-implantitis than screw-retained constructions [51]; similar results were reported for over contoured crowns and supra-structures [52]. A wide emergence profile in the restoration contour was reported to cause an unhealthy state (**Figure 3**) [53].

8.8 Implant-related factors

The titanium particles from the implant surface may be present in the tissues after implant placement and may enhance infection-induced inflammation and

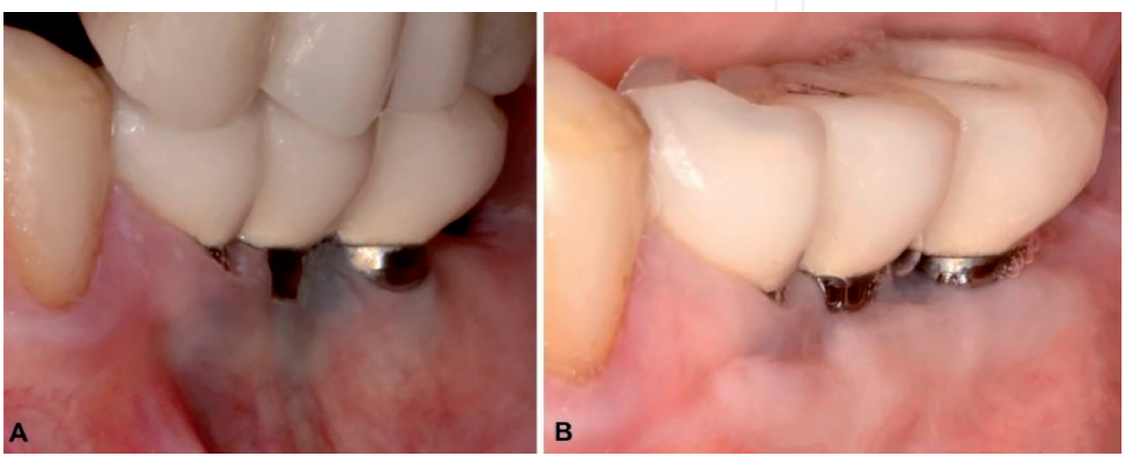

Figure 2.
A. Case showing lack of keratinized gingiva in the implant site. B. After gingival augmentation.

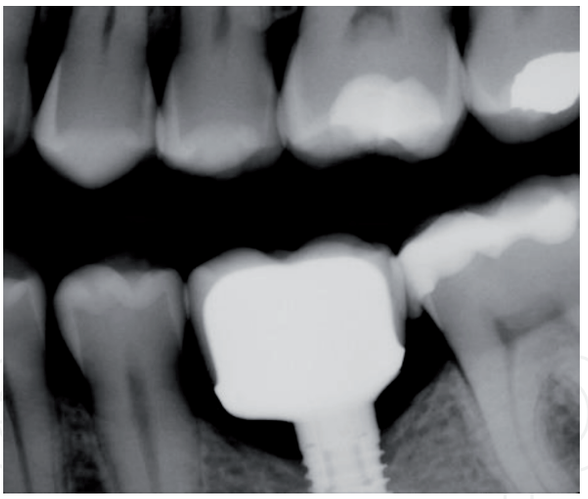

Figure 3.
A case of peri-implantitis consequent to over-contoured restoration.

activate macrophages [54]. Implant surface characteristics vary in terms of topography, surface roughness, and chemical composition. Currently, most implants have a moderately rough surface with improved bone responses during initial healing after implant placement [55]. Marginal bone loss was found to be greater when implants with rough surfaces were used, and turned surfaces generally demonstrated the smallest marginal bone loss [56, 57].

8.8.1 Implant platform switching

The platform switch concept might influence the marginal bone loss. The theory is that the micro-gap is displaced medially causing less bone loss (**Figure 4**) [58–60].

8.8.2 Implant installation

It is advisable to have a minimum thickness of 2-mm bone in the anterior region and at least 1 mm in the posterior region to reduce soft and hard tissue

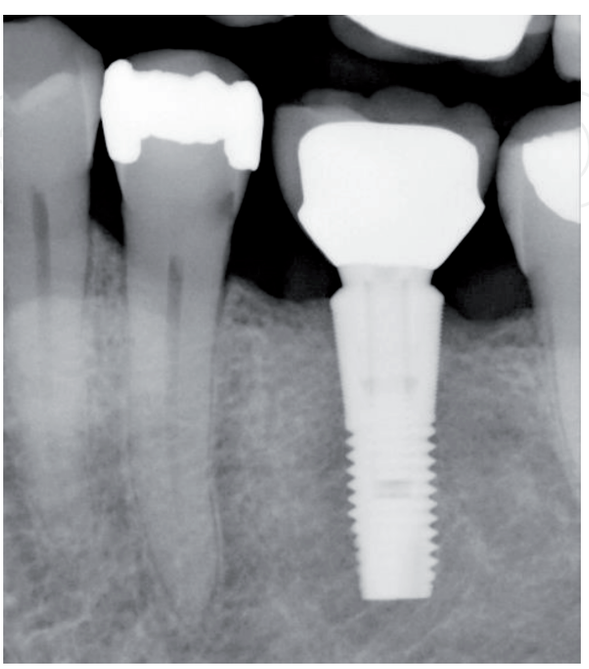

Figure 4.
Platform switching to prevent marginal bone loss and peri-implantitis.

loss. The quality of bone in the region of implant placement is an important factor for the success [61].

8.9 Overload

Clinical signs of occlusal overloads, such as abutment fracture, loss of retention and/or signs of abrasive forces on supra-structures, seem to be an indirect but potential risk. The factors related to occlusal overload are probably related to the location of the implant, the deviation of the axis of the implant, and the incompatibility of the implant dimensions and the prosthesis. Occlusal overload can lead to bone loss around the osseointegrated implants [4]. However, the evidence is limited concerning overload and its influence on the onset or progression of peri-implantitis [41, 62]. In a dog model, occlusal overload did not induce marginal bone loss in implants with a healthy mucosa [63].

8.10 Parafunctional habits-bruxism

Bruxism is a movement disorder of the masticatory system that is characterized among others by teeth grinding and clenching during sleep as well as during wakefulness. Since there is no periodontal ligament between the implant and surrounding bone, the occlusal load is directly transmitted [64]. Even though bruxism is likely to be a risk factor for mechanical complications in the implant periphery, it is unlikely to be a potential risk factor for biological complications [65].

8.11 Alcohol consumption

Alcohol consumption was investigated in one prospective study, which showed that an intake of more than 10 g of alcohol per day was related to peri-implantitis bone loss, as well as tobacco use, plaque, and inflammation [66].

8.12 Iatrogenic factors

The proposed potential risk of iatrogenic factors for the initiation and progression of peri-implantitis caused by implant mal-positioning, surgical trauma, and inadequate restoration abutment seating has not yet been clearly investigated [67].

9. Treatment

9.1 Treatment of peri-implant mucositis

The main goal is to detoxify the contaminated implant surface. Peri-implant mucositis can be managed by non-surgical methods. Methods such as mechanical implant cleaning with titanium or plastic curettes, ultrasonics, or air polishing can be used. Photodynamic therapy as well as local antiseptic medication such as chlorhexidine gluconate, hydrogen peroxide, sodium percarbonate, and povidone-iodine can be used [68–70].

9.2 Treatment of peri-implantitis

The management of peri-implantitis relies on strategies of disinfection such as debridement with curettes and use of local/systemic broad-spectrum antibiotics

associated or not with anti-infective solutions, such as used for chemical plaque control. The strategy is to disinfect and to reduce the inflammation as well as restoration of the peri-implant tissue lost due to the disease progression, usually with regenerative approaches using biologics and/or growth factors. The treatment of peri-implant infections comprises conservative and surgical approaches. Depending on the severity of the peri-implant disease, either a nonsurgical therapy alone or a combined with the surgical method can be used to resolve the situation.

9.3 Non-surgical therapy

Manual treatment approaches using curettes, ultrasonic and air polishing systems, laser-supported, and photodynamic therapy are used along with medications.

9.4 Mechanical therapy

The bleeding from the site can be controlled either with piezoelectric scalers as well as with hand instruments [71]. The manual curetting of the area can be done using special curettes made of Teflon, carbon, plastic, and titanium curettes than the conventional curettes to protect the implant surfaces [72, 73]. The efficiency of the ultrasonic curettage can be supplemented with the air polishing systems [74–77]. Though the abrasive air polishing medium can modify the surface of implants, the cell response and healing were compromised probably due to the contamination of the implant surface [74, 76]. The extent of re-osseointegration of titanium implants after air polishing therapy has been reported between 39 and 46% with increased clinical implant attachment and pocket depth reduction [75]. The air polishing systems such as hydroxylapatite/tricalcium phosphate, hydroxylapatite, glycine, titanium dioxide, water and air, phosphoric acid can be used depending on the surface topography of implants [74, 77].

9.5 Decontamination of the surface of the implant

Decontamination of the root surface is done by various methods such as air powder flow, saline wash, citric acid, laser, and hydrogen peroxide [78]. The electrochemical decontamination of the surface of the implant is an innovative technique that is being tested in preclinical studies [79]. Rubber cups have been shown to smoothen the titanium surface and significantly decrease roughness by removing surface debris. Polishing the implant surfaces with pumice and a rubber cup combined with irrigation with chlorhexidine and systemic antibiotics results in the reduction of anaerobic bacteria and bleeding scores in patients with peri-implantitis [80].

9.6 Laser therapy

Laser treatment using CO_2, diode-, Er:YAG- (erbium-doped: yttrium-aluminum-garnet), and Er, Cr: YSGG- (erbium, chromium-doped: yttrium-scandium-gallium-garnet) lasers are used in the treatment of peri-implant diseases [81, 82]. The use of Er:YAG lasers showed significantly better results than mechanical methods in terms of bleeding at peri-implantitis [83]. Er:YAG and Er, Cr: YAG with a wavelength of 3 microns can reduce biofilms up to 90%, but in contrast to most mechanical therapies, any biological compatibilities and cell stimulatory properties cannot be re-induced [84]. The CO_2 excimer laser was effective in reducing the anaerobic bacteria [85].

9.7 Photodynamic therapy

Photodynamic therapy has to be considered as an additional treatment option in peri-implantitis. Photodynamic therapy generates reactive oxygen species by multiplicity with help of a high-energy single-frequency light in combination with photosensitizers. In a wavelength range of 580–1400 nm and toluidine blue-concentrations between 10 and 50 μg/mL, photodynamic therapy generates bactericide effects against aerobic and anaerobic bacteria such as *Aggregatibacter actinomycetemcomitans*, *Porphyromonas gingivalis*, *Prevotella intermedia*, *Streptococcus mutans*, *Enterococcus faecalis* [86, 87]. An improvement in both clinical attachment and the bleeding index was observed on a moderate and severe peri-implantitis with phototherapy [88]. Photodynamic therapy has been tried as an adjunctive to manual debridement and local chemotherapeutic agents [89].

9.8 Surgical therapy

Surgical techniques may include open flap debridement with removal of the inflammatory tissue as well as mechanical and chemical decontamination of the exposed implant surface. Recontouring of the bony architecture and smoothing of the implant surface may improve infection control [90]. The surgical flap helps in comprehensive debridement and decontamination of the affected implant. The surgical resection is generally confined to implants placed in non-esthetic sites [91].

9.9 Regenerative approaches

Regenerative procedures using a membrane and bone graft substitutes attempting to partially fill the bony defects caused by peri-implantitis can be successful [92]. Therapy of peri-implantitis followed by regular supportive care resulted in favorable clinical improvements and stable peri-implant bone levels in the majority of patients according to a systematic review (**Figure 5**) [93].

9.10 Resective therapy

Resective surgery has been shown to be effective in the reduction of BOP, probing depths and clinical signs of inflammation. The basic principles include the elimination of the peri-implant osseous defect using ostectomy and osteoplasty as well as bacterial decontamination. Additionally, smoothening and polishing of the

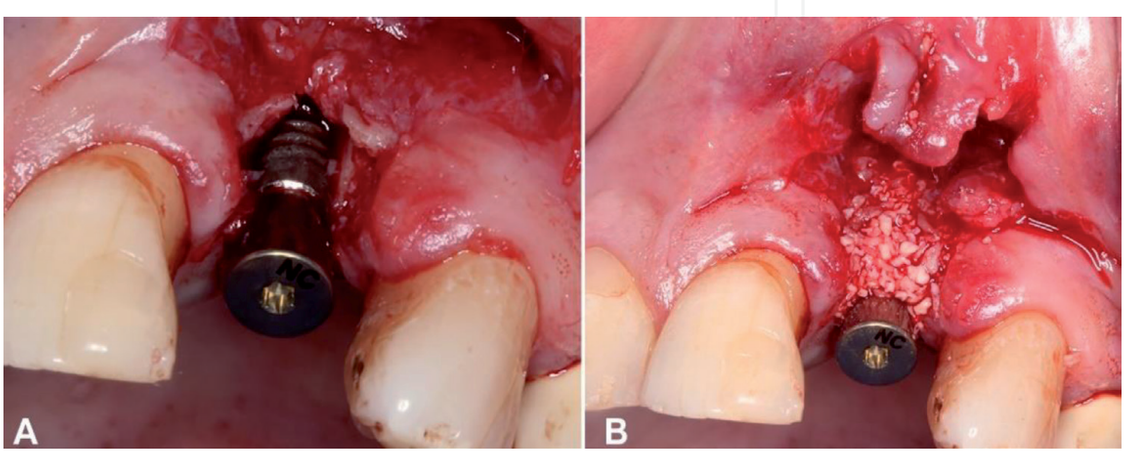

Figure 5.
A case of peri-implantitis treated with bone augmentation.

supracrestal implant surface may be done. Surgical pocket elimination and bone recontouring in combination with plaque control before and after surgery showed effective in treating peri-implantitis [94].

10. Prevention and maintenance

Besides, a maintenance program with regular evaluation of the peri-implant probing depths, supportive professional implant cleaning, and oral hygiene training should be an integral part of every post-operative care after implant insertion [95]. The establishment of an adequate oral hygiene should, therefore, be considered as the key issue of the prevention of peri-implantitis infections.

11. Conclusion

Peri-implantitis is an inflammatory disease of microbial origin causing bone loss around the implant, which could lead to the loss of the implant. The etiology of peri-implantitis is associated with a complex microbial biofilm and risk factors such as smoking and diabetes. Occlusal overloading, osteoporosis, and other factors compromising the surgical site might adversely affect the severity of the destruction of the peri-implant tissue. Several surgical and non-surgical therapeutic approaches have been proposed to manage this complex-multifactorial condition. Anti-infective and regenerative therapeutic strategies were used to restore the peri-implant health as well as to achieve new bone-to-implant contact.

Conflict of interest

The authors declare no conflict of interest.

Author details

Amer Shatta[1*] and Sukumaran Anil[1,2]

1 Department of Dentistry, Oral Health Institute, Hamad Medical Corporation, Doha, Qatar

2 College of Dental Medicine, Qatar University, Doha, Qatar

*Address all correspondence to: ashatta@hamad.qa

References

[1] Bouri A Jr, Bissada N, Al-Zahrani MS, Faddoul F, Nouneh I. Width of keratinized gingiva and the health status of the supporting tissues around dental implants. The International Journal of Oral & Maxillofacial Implants. 2008;**23**(2):323-326

[2] Shatta A, Bissada NF, Ricchetti P, Paes A, Demko C. Impact of implant and site characteristics on the pattern of bone loss in peri-implantitis. The International Journal of Oral & Maxillofacial Implants. 2019;**34**(6):1475-1481

[3] Esposito M, Hirsch JM, 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

[4] 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

[5] Lindhe J, Meyle J. Group DoEWoP: Peri-implant diseases: Consensus Report of the Sixth European Workshop on Periodontology. Journal of Clinical Periodontology. 2008;**35**(8 Suppl):282-285

[6] Berglundh T, Armitage G, Araujo MG, Avila-Ortiz G, Blanco J, Camargo PM, et al. Peri-implant diseases and conditions: Consensus report of workgroup 4 of the 2017 World Workshop on the Classification of Periodontal and Peri-Implant Diseases and Conditions. Journal of Clinical Periodontology. 2018;**45**(S20):S286-S291

[7] Mombelli A, Lang NP. The diagnosis and treatment of peri-implantitis. Periodontology 2000. 1998;**17**:63-76

[8] Sorsa T, Tervahartiala T, Leppilahti J, Hernandez M, Gamonal J, Tuomainen AM, et al. Collagenase-2 (MMP-8) as a point-of-care biomarker in periodontitis and cardiovascular diseases. Therapeutic response to non-antimicrobial properties of tetracyclines. Pharmacological Research. 2011;**63**(2):108-113

[9] Alassiri S, Parnanen P, Rathnayake N, Johannsen G, Heikkinen AM, Lazzara R, et al. The ability of quantitative, specific, and sensitive point-of-care/chair-side oral fluid immunotests for aMMP-8 to detect periodontal and peri-implant diseases. Disease Markers. 2018;**2018**:1306396

[10] Froum SJ, Rosen PS. A proposed classification for peri-implantitis. The International Journal of Periodontics & Restorative Dentistry. 2012;**32**(5):533-540

[11] Atieh MA, Alsabeeha NH, Faggion CM Jr, Duncan WJ. The frequency of peri-implant diseases: A systematic review and meta-analysis. Journal of Periodontology. 2013;**84**(11):1586-1598

[12] Derks J, Tomasi C. Peri-implant health and disease. A systematic review of current epidemiology. Journal of Clinical Periodontology. 2015;**42**(Suppl 16):S158-S171

[13] Rakic M, Galindo-Moreno P, Monje A, Radovanovic S, Wang HL, Cochran D, et al. How frequent does peri-implantitis occur? A systematic review and meta-analysis. Clinical Oral Investigations. 2018;**22**(4):1805-1816

[14] Casado PL, Villas-Boas R, de Mello W, Duarte ME, Granjeiro JM. Peri-implant disease and chronic periodontitis: is interleukin-6 gene promoter polymorphism the common risk factor in a Brazilian population?

The International Journal of Oral & Maxillofacial Implants. 2013;**28**(1):35-43

[15] Rinke S, Ohl S, Ziebolz D, Lange K, Eickholz P. Prevalence of periimplant disease in partially edentulous patients: a practice-based cross-sectional study. Clinical Oral Implants Research. 2011;**22**(8):826-833

[16] Charalampakis G, Leonhardt A, Rabe P, Dahlen G. Clinical and microbiological characteristics of peri-implantitis cases: a retrospective multicentre study. Clinical Oral Implants Research. 2012;**23**(9):1045-1054

[17] Mir-Mari J, Mir-Orfila P, Figueiredo R, Valmaseda-Castellon E, Gay-Escoda C. Prevalence of peri-implant diseases. A cross-sectional study based on a private practice environment. Journal of Clinical Periodontology. 2012;**39**(5):490-494

[18] Marrone A, Lasserre J, Bercy P, Brecx MC. Prevalence and risk factors for peri-implant disease in Belgian adults. Clinical Oral Implants Research. 2013;**24**(8):934-940

[19] Corbella S, Del Fabbro M, Taschieri S, De Siena F, Francetti L. Clinical evaluation of an implant maintenance protocol for the prevention of peri-implant diseases in patients treated with immediately loaded full-arch rehabilitations. International Journal of Dental Hygiene. 2011;**9**(3):216-222

[20] Costa FO, Takenaka-Martinez S, Cota LO, Ferreira SD, Silva GL, Costa JE. Peri-implant disease in subjects with and without preventive maintenance: A 5-year follow-up. Journal of Clinical Periodontology. 2012;**39**(2):173-181

[21] Cecchinato D, Parpaiola A, Lindhe J. A cross-sectional study on the prevalence of marginal bone loss among implant patients. Clinical Oral Implants Research. 2013;**24**(1):87-90

[22] Cecchinato D, Parpaiola A, Lindhe J. Mucosal inflammation and incidence of crestal bone loss among implant patients: A 10-year study. Clinical Oral Implants Research. 2014;**25**(7):791-796

[23] Dvorak G, Arnhart C, Heuberer S, Huber CD, Watzek G, Gruber R. Peri-implantitis and late implant failures in postmenopausal women: A cross-sectional study. Journal of Clinical Periodontology. 2011;**38**(10):950-955

[24] Gotfredsen K. A 10-year prospective study of single tooth implants placed in the anterior maxilla. Clinical Implant Dentistry and Related Research. 2012;**14**(1):80-87

[25] Casado PL, Pereira MC, Duarte ME, Granjeiro JM. History of chronic periodontitis is a high risk indicator for peri-implant disease. Brazilian Dental Journal. 2013;**24**(2):136-141

[26] Meyle J, Gersok G, Boedeker RH, Gonzales JR. Long-term analysis of osseointegrated implants in non-smoker patients with a previous history of periodontitis. Journal of Clinical Periodontology. 2014;**41**(5):504-512

[27] Heitz-Mayfield LJ, Lang NP. Comparative biology of chronic and aggressive periodontitis vs. peri-implantitis. Periodontology 2000. 2010;**53**:167-181

[28] Berglundh T, Lindhe J, Ericsson I, Liljenberg B. Enhanced gingivitis in the deciduous and permanent dentition. An experimental study in the dog. Journal of Clinical Periodontology. 1992;**19**(2):135-142

[29] Pontoriero R, Tonelli MP, Carnevale G, Mombelli A, Nyman SR, Lang NP. Experimentally induced peri-implant mucositis. A clinical study in humans. Clinical Oral Implants Research. 1994;**5**(4):254-259

[30] Ericsson I, Berglundh T, Marinello C, Liljenberg B, Lindhe J. Long-standing plaque and gingivitis at implants and teeth in the dog. Clinical Oral Implants Research. 1992;**3**(3):99-103

[31] Salvi GE, Aglietta M, Eick S, Sculean A, Lang NP, Ramseier CA. Reversibility of experimental peri-implant mucositis compared with experimental gingivitis in humans. Clinical Oral Implants Research. 2012;**23**(2):182-190

[32] Abrahamsson I, Berglundh T, Glantz PO, Lindhe J. The mucosal attachment at different abutments. An experimental study in dogs. Journal of Clinical Periodontology. 1998;**25**(9):721-727

[33] Carcuac O, Abrahamsson I, Albouy JP, Linder E, Larsson L, Berglundh T. Experimental periodontitis and peri-implantitis in dogs. Clinical Oral Implants Research. 2013;**24**(4):363-371

[34] Lindhe J, Berglundh T, Ericsson I, Liljenberg B, Marinello C. Experimental breakdown of peri-implant and periodontal tissues. A study in the beagle dog. Clinical Oral Implants Research. 1992;**3**(1):9-16

[35] Berglundh T, Zitzmann NU, Donati M. Are peri-implantitis lesions different from periodontitis lesions? Journal of Clinical Periodontology. 2011;**38**(s11):188-202

[36] Carcuac O, Berglundh T. Composition of human peri-implantitis and periodontitis lesions. Journal of Dental Research. 2014;**93**(11):1083-1088

[37] Gualini F, Berglundh T. Immunohistochemical characteristics of inflammatory lesions at implants. Journal of Clinical Periodontology. 2003;**30**(1):14-18

[38] Roccuzzo M, Bonino F, Aglietta M, Dalmasso P. Ten-year results of a three arms prospective cohort study on implants in periodontally compromised patients. Part 2: Clinical results. Clinical Oral Implants Research. 2012;**23**(4):389-395

[39] Karoussis IK, Salvi GE, Heitz-Mayfield LJ, Bragger U, Hammerle 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

[40] Derks J, Schaller D, Hakansson J, Wennstrom JL, Tomasi C, Berglundh T. Peri-implantitis—Onset and pattern of progression. Journal of Clinical Periodontology. 2016;**43**(4):383-388

[41] Schwarz F, Derks J, Monje A, Wang HL. Peri-implantitis, 45. Journal of Clinical Periodontology, Suppl. 2018;**20**(S20):S246-S266

[42] Laine ML, Leonhardt A, Roos-Jansaker AM, Pena AS, van Winkelhoff AJ, Winkel EG, et al. IL-1RN gene polymorphism is associated with peri-implantitis. Clinical Oral Implants Research. 2006;**17**(4):380-385

[43] Feloutzis A, Lang NP, Tonetti MS, Burgin W, Bragger U, Buser D, et al. IL-1 gene polymorphism and smoking as risk factors for peri-implant bone loss in a well-maintained population. Clinical Oral Implants Research. 2003;**14**(1):10-17

[44] Venza I, Visalli M, Cucinotta M, De Grazia G, Teti D, Venza M. Proinflammatory gene expression at chronic periodontitis and peri-implantitis sites in patients with or without type 2 diabetes. Journal of Periodontology. 2010;**81**(1):99-108

[45] Ferreira SD, 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

[46] Naujokat H, Kunzendorf B, Wiltfang J. Dental implants and diabetes mellitus—A systematic review. International Journal of Implant Dentistry. 2016;**2**(1):5

[47] Schwarz F, Becker K, Sahm N, Horstkemper T, Rousi K, Becker J. The prevalence of peri-implant diseases for two-piece implants with an internal tube-in-tube connection: A cross-sectional analysis of 512 implants. Clinical Oral Implants Research. 2017;**28**(1):24-28

[48] Roos-Jansaker AM, Lindahl C, Renvert H, Renvert S. Nine- to fourteen-year follow-up of implant treatment. Part I: Implant loss and associations to various factors. Journal of Clinical Periodontology. 2006;**33**(4):283-289

[49] Strietzel FP, Reichart PA, Kale A, Kulkarni M, Wegner B, Kuchler I. Smoking interferes with the prognosis of dental implant treatment: A systematic review and meta-analysis. Journal of Clinical Periodontology. 2007;**34**(6):523-544

[50] Roccuzzo M, Grasso G, Dalmasso P. Keratinized mucosa around implants in partially edentulous posterior mandible: 10-year results of a prospective comparative study. Clinical Oral Implants Research. 2016;**27**(4):491-496

[51] Staubli N, Walter C, Schmidt JC, Weiger R, Zitzmann NU. Excess cement and the risk of peri-implant disease—A systematic review. Clinical Oral Implants Research. 2017;**28**(10):1278-1290

[52] Becker CM, Kaldahl WB. Current theories of crown contour, margin placement, and pontic design. The Journal of Prosthetic Dentistry. 1981;**45**(3):268-277

[53] Katafuchi M, Weinstein BF, Leroux BG, Chen YW, Daubert DM. Restoration contour is a risk indicator for peri-implantitis: A cross-sectional radiographic analysis. Journal of Clinical Periodontology. 2018;**45**(2):225-232

[54] Pettersson M, Pettersson J, Johansson A, Molin Thoren M. Titanium release in peri-implantitis. Journal of Oral Rehabilitation. 2019;**46**(2):179-188

[55] Albrektsson T, Wennerberg A. Oral implant surfaces: Part 1—Review focusing on topographic and chemical properties of different surfaces and in vivo responses to them. The International Journal of Prosthodontics. 2004;**17**(5):536-543

[56] Baelum V, Ellegaard B. Implant survival in periodontally compromised patients. Journal of Periodontology. 2004;**75**(10):1404-1412

[57] Wennerberg A, Albrektsson T, Chrcanovic B. Long-term clinical outcome of implants with different surface modifications. European Journal of Oral Implantology. 2018;**11**(Suppl 1):S123-S136

[58] Nguyen-Hieu T, Borghetti A, Aboudharam G. Peri-implantitis: From diagnosis to therapeutics. Journal of Investigative and Clinical Dentistry. 2012;**3**(2):79-94

[59] Cappiello M, Luongo R, Di Iorio D, Bugea C, Cocchetto R, Celletti R. Evaluation of peri-implant bone loss around platform-switched implants. The International Journal of Periodontics & Restorative Dentistry. 2008;**28**(4):347-355

[60] Lazzara RJ, Porter SS. Platform switching: A new concept in implant dentistry for controlling postrestorative

crestal bone levels. The International Journal of Periodontics & Restorative Dentistry. 2006;**26**(1):9-17

[61] Quoc JB, Vang A, Evrard L. Peri-implant bone loss at implants placed in preserved alveolar bone versus implants placed in native bone: A retrospective radiographic study. The Open Dentistry Journal. 2018;**12**:529-545

[62] Klinge B, Meyle J, Working G. Peri-implant tissue destruction. The Third EAO Consensus Conference 2012. Clinical Oral Implants Research. 2012;**23**(Suppl 6):108-110

[63] Heitz-Mayfield LJ, Schmid B, Weigel C, Gerber S, Bosshardt DD, Jonsson J, et al. Does excessive occlusal load affect osseointegration? An experimental study in the dog. Clinical Oral Implants Research. 2004;**15**(3):259-268

[64] Kahramanoglu E, Kulak-Ozkan Y. Marginal and internal adaptation of different superstructure and abutment materials using two different implant systems for five-unit implant-supported fixed partial dentures: An in vitro study. The International Journal of Oral & Maxillofacial Implants. 2013;**28**(5):1207-1216

[65] Zupnik J, Kim SW, Ravens D, Karimbux N, Guze K. Factors associated with dental implant survival: A 4-year retrospective analysis. Journal of Periodontology. 2011;**82**(10):1390-1395

[66] Galindo-Moreno P, Fauri M, Avila-Ortiz G, Fernandez-Barbero JE, Cabrera-Leon A, Sanchez-Fernandez E. Influence of alcohol and tobacco habits on peri-implant marginal bone loss: A prospective study. Clinical Oral Implants Research. 2005;**16**(5):579-586

[67] Lang NP, Berglundh T. Working Group 4 of Seventh European Workshop on P: Periimplant diseases: Where are we now?—Consensus of the Seventh European Workshop on Periodontology. Journal of Clinical Periodontology. 2011;**38**(Suppl 11):178-181

[68] Heitz-Mayfield LJ, Salvi GE, Botticelli D, Mombelli A, Faddy M, Lang NP, et al. Anti-infective treatment of peri-implant mucositis: A randomised controlled clinical trial. Clinical Oral Implants Research. 2011;**22**(3):237-241

[69] Hallstrom H, Persson GR, Lindgren S, Olofsson M, Renvert S. Systemic antibiotics and debridement of peri-implant mucositis. A randomized clinical trial. Journal of Clinical Periodontology. 2012;**39**(6):574-581

[70] Zeza B, Pilloni A. Peri-implant mucositis treatments in humans: A systematic review. Annali di Stomatologia (Roma). 2012;**3**(3-4):83-89

[71] Renvert S, Samuelsson E, Lindahl C, Persson GR. Mechanical non-surgical treatment of peri-implantitis: A double-blind randomized longitudinal clinical study. I: Clinical results. Journal of Clinical Periodontology. 2009;**36**(7):604-609

[72] Augthun M, Tinschert J, Huber A. In vitro studies on the effect of cleaning methods on different implant surfaces. Journal of Periodontology. 1998;**69**(8):857-864

[73] Unursaikhan O, Lee JS, Cha JK, Park JC, Jung UW, Kim CS, et al. Comparative evaluation of roughness of titanium surfaces treated by different hygiene instruments. Journal of Periodontal and Implant Science. 2012;**42**(3):88-94

[74] Tastepe CS, Liu Y, Visscher CM, Wismeijer D. Cleaning and modification of intraorally contaminated titanium discs with calcium phosphate powder abrasive treatment. Clinical Oral Implants Research. 2013;**24**(11):1238-1246

[75] Tastepe CS, van Waas R, Liu Y, Wismeijer D. Air powder abrasive treatment as an implant surface cleaning method: A literature review. The International Journal of Oral & Maxillofacial Implants. 2012;**27**(6):1461-1473

[76] Sahm N, Becker J, Santel T, Schwarz F. Non-surgical treatment of peri-implantitis using an air-abrasive device or mechanical debridement and local application of chlorhexidine: A prospective, randomized, controlled clinical study. Journal of Clinical Periodontology. 2011;**38**(9):872-878

[77] Louropoulou A, Slot DE, Van der Weijden F. The effects of mechanical instruments on contaminated titanium dental implant surfaces: A systematic review. Clinical Oral Implants Research. 2014;**25**(10):1149-1160

[78] Ntrouka V, Hoogenkamp M, Zaura E, van der Weijden F. The effect of chemotherapeutic agents on titanium-adherent biofilms. Clinical Oral Implants Research. 2011;**22**(11):1227-1234

[79] Mohn D, Zehnder M, Stark WJ, Imfeld T. Electrochemical disinfection of dental implants—A proof of concept. PLoS One. 2011;**6**(1):e16157

[80] Schwarz F, Schmucker A, Becker J. Efficacy of alternative or adjunctive measures to conventional treatment of peri-implant mucositis and peri-implantitis: A systematic review and meta-analysis. International Journal of Implant Dentistry. 2015;**1**(1):22

[81] Schwarz F, Sculean A, Rothamel D, Schwenzer K, Georg T, Becker J. Clinical evaluation of an Er:YAG laser for nonsurgical treatment of peri-implantitis: A pilot study. Clinical Oral Implants Research. 2005;**16**(1):44-52

[82] Mailoa J, Lin GH, Chan HL, MacEachern M, Wang HL. Clinical outcomes of using lasers for peri-implantitis surface detoxification: A systematic review and meta-analysis. Journal of Periodontology. 2014;**85**(9):1194-1202

[83] Persson GR, Roos-Jansaker AM, Lindahl C, Renvert S. Microbiologic results after non-surgical erbium-doped:yttrium, aluminum, and garnet laser or air-abrasive treatment of peri-implantitis: A randomized clinical trial. Journal of Periodontology. 2011;**82**(9):1267-1278

[84] Yamamoto A, Tanabe T. Treatment of peri-implantitis around TiUnite-surface implants using Er:YAG laser microexplosions. The International Journal of Periodontics & Restorative Dentistry. 2013;**33**(1):21-30

[85] Deppe H, Horch HH, Schrodl V, Haczek C, Miethke T. Effect of 308-nm excimer laser light on peri-implantitis-associated bacteria: An in vitro investigation. Lasers in Medical Science. 2007;**22**(4):223-227

[86] Al-Ahmad A, Tennert C, Karygianni L, Wrbas KT, Hellwig E, Altenburger MJ. Antimicrobial photodynamic therapy using visible light plus water-filtered infrared-A (wIRA). Journal of Medical Microbiology. 2013;**62**(Pt 3):467-473

[87] Meisel P, Kocher T. Photodynamic therapy for periodontal diseases: State of the art. Journal of Photochemistry and Photobiology. B. 2005;**79**(2):159-170

[88] Deppe H, Mucke T, Wagenpfeil S, Kesting M, Sculean A. Nonsurgical antimicrobial photodynamic therapy in moderate vs severe peri-implant defects: A clinical pilot study. Quintessence International. 2013;**44**(8):609-618

[89] Bassetti M, Schar D, Wicki B, Eick S, Ramseier CA, Arweiler NB, et al. Anti-infective therapy of

peri-implantitis with adjunctive local drug delivery or photodynamic therapy: 12-month outcomes of a randomized controlled clinical trial. Clinical Oral Implants Research. 2014;**25**(3):279-287

[90] Schou S, Berglundh T, Lang NP. Surgical treatment of peri-implantitis. The International Journal of Oral & Maxillofacial Implants. 2004;**19**(Suppl):140-149

[91] Prathapachandran J, Suresh N. Management of peri-implantitis. Dental Research Journal. 2012;**9**(5):516-521

[92] Roccuzzo M, Layton DM, Roccuzzo A, Heitz-Mayfield LJ. Clinical outcomes of peri-implantitis treatment and supportive care: A systematic review. Clinical Oral Implants Research. 2018;**29**(Suppl 16):331-350

[93] Sahrmann P, Attin T, Schmidlin PR. Regenerative treatment of peri-implantitis using bone substitutes and membrane: A systematic review. Clinical Implant Dentistry and Related Research. 2011;**13**(1):46-57

[94] Serino G, Strom C. Peri-implantitis in partially edentulous patients: association with inadequate plaque control. Clinical Oral Implants Research. 2009;**20**(2):169-174

[95] Khammissa RA, Feller L, Meyerov R, Lemmer J. Peri-implant mucositis and peri-implantitis: Clinical and histopathological characteristics and treatment. SADJ. 2012;**67**(3):122, 124-126