

Prevention of Peri-Implantitis: A Narrative Review

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Abstract

With the discovery of osseointegration and advancement in dental materials dental implants provide superior support, stability and retention for prosthetic replacement of missing teeth than any available prosthetic option. But with the use of implants, an associated biological complication of peri-implant disease is seen in 48% of cases. Hence, this review aims to summarize the risk factors associated with peri-implantitis and highlights current prevention strategies available and those to be further researched to minimise the incidence and severity of peri-implant disease and enhance longevity of implants.

Keywords: Peri-Implantitis; Implants; Prevention

Background

Dental implant therapy is currently a popular treatment modality for the rehabilitation of partial and complete edentulism [1,2]. According to the American Academy of Implant Dentistry, around 3 million Americans utilize dental implants with an increasing number of 5,00,000 every year [3-5]. Dental implants mimic the root structure of the tooth osseointegrating with the surrounding bone, thereby extending superior support, stability and retention to the attached prosthesis unlike other available options for tooth replacement [6].

Based on the particulars and requirements of the patients, fixed or removable prosthesis can be fabricated for implants that can range from single tooth replacements to partial or complete dentures [5]. Immediate loading of implants is also possible that assists in decreasing overall treatment time for patients. Due to its endosseous nature, implants preserve the existing bone, which is a basic requirement for any prosthetic rehabilitation [5]. In case of implant prosthesis, the teeth adjacent to the edentulous span are not used as abutments, thus eliminating the need to prepare them. With a success rate of 95% for 5 to 10 years as demonstrated in long-term studies, implants offer a permanent and durable prosthetic solution to edentulism [7-9]. Studies have also shown that implants provide better patient satisfaction and quality of life. Along with the benefits, the complications associated with implant therapy are presently being documented. The placement of implants requires minor surgeries that can lead to immediate surgical complications like excessive bleeding, poor healing and infections [10]. Post implant placement, the implant must be stable and immobile which constitutes primary stability. This primary stabilization then leads to successful osseointegration that constitutes secondary stabilization of the implant [11]. Late complications can occur in the prosthetic and maintenance phase after the implant has successfully osseointegrated. Failure to prevent these complications results in the occurrence of peri-implant disease [12]. Peri-implant disease constitutes peri-mucositis and peri-implantitis [13]. Peri-mucositis is defined as a reversible inflammatory reaction in the soft tissues surrounding an implant in function, whereas peri-implantitis is more severe and is defined as a more profound inflammatory lesion characterized by a deepened peri-implant pocket and loss of supporting bone around a functional implant. In analogy to gingivitis and periodontitis affecting the periodontium of natural teeth, an inflammation and destruction of soft and hard tissues surrounding dental implants is termed as mucositis and peri-implantitis [14,15]. According to the American Academy of Periodontology report, 48% of implants followed from 9 to 14 years of placement showed a prevalence of peri-implant disease. A number of risk factors are associated with peri-implant disease that occurs as a late complication. These complications can eventually lead to implant failure if timely intervention is not sought. Further studies are required to establish the relevancy of risk factors associated with peri-implant disease [15]. However, the Sixth European Convention confirmed the infectious nature

of peri-implant disease and declared it to be treatable. Reviewing the existing therapies available to prevent or reduce the severity of its occurrence and highlighting the need to develop better preventive measures in order to prevent implant failure is the aim of this paper.

Etiopathogenesis

The analogy between gingivitis and peri-mucositis, periodontitis and peri-implantitis with regards to the etiology and host immune response that contributes to the pathogenesis of these conditions has been well established [14]. The key events in the pathogenesis of peri-mucositis involves formation of a biofilm due to the precipitation of salivary glycol-proteins on the transmucosal abutment surface of implant and subsequent microbial colonization that initiates an inflammatory host immune response in the adjacent peri-implant soft tissue cuff [14,16]. This peri-implant soft tissue cuff is fundamentally different from the soft tissue around natural tooth. Unlike natural tooth functional peri-implant epithelial sealing with basal lamina (BL) attachment at the interface of the implant and the adjacent epithelium is lacking and allows bacterial invasion [17]. The biologic width consists of a 2mm long non-keratinized junctional epithelium contacting the implant and a 2mm sub-epithelial connective tissue component that is similar to scar tissue in composition, vasculature and fibre orientation and acts as a seal from the oral microbiome [18]. The collagen fibres that do not attach to the implant surface or run circumferentially like the transeptal fibres [18]. Thus self-limiting ability of the tissue is severely compromised and the inflammatory cell infiltrate extends to the alveolar crest. Peri-mucositis is a reversible condition and does not necessarily progress into peri-implantitis if the biofilm is eliminated in time.

The inflammation pathway is shorter and faster since osseointegrated implants directly contact bone and lack interposed periodontal ligament and cemental tissue [18]. In case of prolonged plaque accumulation, the perio-pathogetic organisms and their products proliferate apically and the accompanying inflammatory cell infiltrate causes soft tissue destruction and resorption of the implant supporting crestal bone leading to pocket formation that characterizes peri-implantitis [18].

To some degree the bacterial strains implicated in periodontitis and peri-implantitis are similar but on the whole the microbiological eco system are distinct. *Prevotella intermedia*, *Aggregatibacter actinomycetemcomitans*, *Porphyromonas gingivalis*, *Bacteroides forsythus*, *Treponema denticola*, *Tannerella forsythia*, *Fusobacterium nucleatum*, *Campylobacter*, *Peptostreptococcus micros* are few species involved in the formation of the biofilm [17]. In addition *Staphylococcus aureus*, enteric species and candidal strains have also been observed in peri-implantitic lesions [18]. Along with the infectious agents, multiple lifestyle, environment and genetic factors play a crucial role in the development of peri-implant disease.

Risk Factors

A number of risk factors have been found to be associated with the development of peri-implantitis. Understanding the impact of these factors on predisposing an individual to peri-implantitis is extremely crucial to improve prevention strategies and therapeutic outcomes. Canullo *et al.* aimed to investigate whether specific predictive profiles for patient-based risk assessment/diagnostics could be applied in different subtypes of peri-implantitis in a sample of fifty-six patients with 332 implants and reported that plaque induced and prosthetically and surgically triggered peri-implantitis are different entities associated with distinguishing predictive profiles [19].

Genetic Predisposition

Lee *et al.* studied the role of genetic polymorphism in 6 patients with severe peri-implantitis and high rates of implant failure [20]. They concluded that various gene sets are indirectly linked to the dysregulation of metal ion concentration like Ca^{2+} and Mn^{2+} that impair the activation of integrins and other factors that govern cell adhesion. Poor cell adhesion affects the process of osseointegration of implants and modifies the host immune response [20]. IL-6 G174C polymorphism has been linked to periodontitis and peri-implantitis. The association between CD14-159 C/T and TNF α -308 A/G polymorphisms with peri-implantitis has been confirmed in a population of 369 Caucasian individuals [21].

Smoking

Smoking was thought to cause vasoconstriction adversely affecting osseointegration, but its effects are mainly seen in the poor healing of the peri-implant soft tissue cuff exposed to tobacco smoke [22]. According to a study by Tsigarida *et al.* smoking directly affects the peri-implant microbiome. While it reduces several health related species of the core microbiome, it is enriched in case of species traditionally regarded as periodontal and/or systemic pathogens predisposing an individual to peri-implantitis and adversely affecting implant longevity [23]. A systematic review has concluded that an implant based meta-analysis revealed a significant risk for peri-implantitis whereas a patient based meta-analysis did not establish the relevancy of smoking as a risk factor in the development of peri implantitis [22,24].

History of periodontitis

A meta-analysis that was carried out by Ramanaukait *et al.* included 14 studies with >5yr follow up of implant patients revealed a higher incidence of peri-implantitis in patients with a previous history of periodontitis although it did not significantly affect

the success rate of implants [25]. In partially edentulous patients, teeth act as a reservoir of perio pathogenic organisms for translocation on the implant surface whereas in fully edentulous patients they are found on the tongue or in saliva. Therefore a history or active periodontitis especially aggressive periodontitis predisposes an individual to the development of peri-implantitis and completion of periodontal therapy must precede implant therapy in such cases.

Poor oral hygiene maintenance

A routine maintenance therapy is mandatory for implant longevity. Lack of patient compliance in following prescribed oral hygiene procedures and skipping recall appointments will lead to plaque accumulation and eventual peri-implant disease. Poor oral hygiene significantly elevates the risk of peri-implantitis [26-28].

Systemic Diseases

A number of systemic diseases are suspected as potential risk factors in the development of peri-implantitis. A study by Monje *et al.* detected the risk of peri-implantitis was about 50% higher in diabetic patients and concluded that diabetes mellitus/hyperglycaemia is associated with greater risk of peri-implantitis, independently of smoking, but not with peri-implant mucositis [29]. Another study by Naujokat found diabetes is not a short-term risk factor rather elevates the risk of peri-implantitis after 6 and more years of implantation [30]. They recommend avoidance of immediate loading of implants since smoking causes delayed osseointegration.

Cardiovascular disease in conjunction with periodontitis is found to increase the risk of peri-implantitis. Caution has been recommended in patients with Sjögren's syndrome and Ectodermal dysplasia especially in case of mandibular implants in the latter. Recently published systematic reviews have failed to confirm or refute osteoporosis, rheumatoid arthritis and Crohn's syndrome as a potential risk factor in the pathogenesis of peri-implantitis highlighting the need for randomized control trials in this regard to help evaluate this possibility [31,32]. HIV does not significantly affect the rate of success of implants. Due to insufficient evidence and small sample size in the studies carried out, the results remain irresolute.

Surgical placement of implants

Maintaining sterile conditions during implantation and restoring carious teeth adjacent to the implant site is extremely crucial to prevent contamination and subsequent infection. To minimize post-surgical complications, pretreatment antibiotic coverage, careful planning of the flap design, gentle manipulation of soft tissue, minimizing bone trauma due to heat produced during drilling and maintenance of flap coverage must be achieved after implantation [33]. Implant placement must be planned based on final prosthesis design.

Prosthetic rehabilitation of implants

Poor implant prosthesis design can preclude adequate accessibility for plaque control and proper clinical evaluation during follow-ups [27,34]. There are several prosthetic factors that can affect the rate of peri implantitis. Overloading can have negative effects on the surrounding tissues of the periodontium Kozlovsky *et al.*, described the effect of overloading on peri-implantitis and reported that in the presence of uninflamed peri-implant mucosa, overloading of implants in the dog model increased bone to implant contact % and slightly reduced marginal bone level. However, resorption did not progress beyond the implant neck and overloading aggravated the plaque-induced bone resorption when peri-implant inflammation was present [35]. Treatment plan must include bone density, implant dimension consideration and soft tissue quality at the site of implantation. The opposing occlusion as well as the restorative material of the prosthesis must be considered during treatment planning. Occlusal overload is known to cause peri-implantitis especially in bruxers [36,37].

Radiotherapy

A meta-analysis of irradiated patients carried out by Chrcanovic *et al.* observed a statistically significant higher implant survival in the irradiated native bone compared to the irradiated grafted bone [38]. Thus radiation in combination with bone graft is a risk factor for peri-implantitis.

Residual cement

In a retrospective analysis by Linkevicius, it was observed that residual cement predisposes a patient to peri-implant disease; the risk is further elevated in case of individuals with a history of periodontitis [39]. Thus in such cases screw retained prosthesis is a better treatment option.

Implant material and design: Micro cavities are present at implant-abutment connection level in two-piece implantsystems, a consequence of current manufacturing limitation that allow bacterial infiltration and inflammation around the neck of the implant [40-42]. Surface modifications creating micro-rough implant surfaces accelerate the osseointegration process of titanium implants. A systematic review and meta-analysis by Rakic *et al.* included 29 papers and reported that the prevalence of peri-implantitis was 18.5% at the patient level and 12.8% at the implant level, as well as, implant surface characteristics could play a major role in the initiation of peri-implantitis [43]. Moreover, the review stated demonstrated a significant association between moderately rough surfaces associated with a low prevalence rate of peri-implantitis.

Preventive measures

Cumulative Interceptive Supportive Therapy (CIST) was presented during a 2002 Consensus Workshop at Berne, Switzerland that constitutes a rigorous approach to monitoring both peri-implant hard and soft tissues to prevent and treat peri-implant disease [44,45].

Prevention of peri-implantitis should start at treatment planning itself. An effective supportive implant therapy program must be planned prior to treatment that constitutes meticulous oral hygiene practices, careful peri-implant examination, reducing any associated risk factors and periodic removal of microbial deposits from the implants. A patient centered recall program of supportive implant therapy must be followed with a minimum of 3-6 months recall interval, can help return the mucosa to a healthy state and continue to maintain its health to prevent the development of peri-implantitis. During recall when probing, plastic, graphite, nylon, or Teflon®-coated instruments should be used instead of metal with minimal probing force to prevent damage to the peri-implant soft tissue cuff and implant surface. Loss of the titanium oxide layer present on the implant surface leads to surface roughness and corrosion that acts as a site for plaque accumulation.

To prevent or minimize plaque accumulation around the implant site novel techniques of controlled localized delivery of antibiotics and systemic antibiotics are being researched. A study by Lan *et al.* demonstrated an effective technique for the controlled release of metronidazole using custom fabricated biodegradable poly ϵ -caprolactone alginate rings at the implant site [46]. A study by Bhattarai *et al.* used Chitosan gold nanoparticles (Ch-GNPs) a gene delivery material to carry anti-inflammatory peroxisome proliferator activated receptor gamma molecules (PPAR γ cDNA) into the required areas of the implant surfaces, thus aiding to inhibit inflammation and promote osteoblast function [47].

Various studies have suggested coating titanium implant surface with zinc oxidehydroxyapatite nanoparticles or an erythritol chlorhexidine combination or engineered chimeric peptides or a multilayer coating with AMPCol or disinfecting the surface with titanium brush and photodynamic therapy, to prevent the formation of a biofilm [48]. Sugano *et al.* discussed in his review paper the use of probiotic *Lactobacillus reuteri* to create a biofilm that protected the oral tissues against the action of periodontal pathogenic bacteria [49]. A study by Lasserre *et al.* shows the promising effect of low direct current on the detachment of implant adherent biofilm. Bacteriophage therapy is a new development in prevention of biofilm formation [50].

To combat the lack of a functional epithelial seal around implants Maeno *et al.* studied the barrier function of platelet induced epithelial sheet on titanium implants [51]. They carried out surface modification of implant with protease-activated receptor 4-activating peptide (PAR4-AP) incubated with platelet rich plasma (PRP) that activated platelets of PRP releasing type IV collagen. They then seeded the implant surface with human gingival epithelial cells to form an epithelial sheet with basal lamina that is highly resistant to bacterial attachment.

Ongoing research is aimed at improving the current fabrication limitations in implant design and material. A study by Pautke *et al.* demonstrated that implants manufactured with gap-free abutments using a shape memory alloy nitinol showed significantly reduced bacterial leakage compared to conventional implants [52]. This improvement could minimize peri-implantitis and consequently enhance longevity of dental implants. The incidence of peri-implantitis with zirconia implants is found to be very low due to its excellent biocompatibility and low affinity to plaque. Also zirconia implants are manufactured as one-piece implant system that is seen as beneficial. Further clinical investigations must be carried out to identify possible biological and mechanical factors associated with this system to reach a consensus [53,54].

Newer oral hygiene aids are being introduced to maintain optimal periodontal health. Water irrigation units are found to be beneficial in implant maintenance. A study by Sreenivasan *et al.* concluded that a triclosan/copolymer dentrifice was more effective in plaque control compared to a fluoride dentrifice [55]. Plastic ultrasonic scalers and curettes must be used to remove hard deposits on the implant surface. Air polish systems using hydroxylapatite/tricalcium phosphate as a medium is least abrasive and found to remove plaque without altering the surface of the implant.

Summary

A gold standard approach is currently not available to prevent peri-implantitis. A rigorous patient centered recall program to maintain peri-implant tissue health successfully reduces plaque accumulation but does not entirely prevent peri-implantitis. To make implant therapy a more predictable treatment modality research must be focused in areas pertaining to identification of risk factors, better prosthetic rehabilitation of implants, efficacy of interproximal cleaning aids, prevention of biofilm formation and improvement in implant design and material.

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