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CLINICAL PERIODONTICS (Y STATHOPOULOU, SECTION EDITOR)

Current Protocols for the Treatment of Peri-implantitis

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Abstract

Purpose of Review Peri-implant diseases are becoming a major problem in modern dentistry. A clear understanding of the pathogenesis of peri-implant diseases may provide key aspects for decision-making on their approach and obtaining predictable results. The purpose of the present article is to provide a narrative review of current protocols (2015–present) used for treatment of peri-implantitis.

Recent Findings Current evidence reflects the level of diagnostic and therapeutic complexity; and multifactorial effect of conditions associated with peri-implant mucositis and peri-implantitis. Non-surgical therapy, by means of mechanical detoxification with or without adjuncts, has proven somehow effective for the treatment of mild forms of peri-implantitis. Conversely, open flap mechanical debridement with resective and/or regenerative treatment modalities have been advocated more towards moderate-to-severe forms. There is a lack of evidence to support the use of adjuncts (e.g. systemic/locally-delivered antibiotics, antimicrobial mouth rinses, biologic agents, laser therapy, antimicrobial photodynamic therapy, soft tissue augmentation) with conventional mechanical therapy upon the long-term outcomes after the peri-implantitis treatment.

Summary Emerging long-term results found surgical outcomes after peri-implantitis therapy to remain unpredictable in arresting inflammation, but effective in preventing further bone destruction and implant loss. In the presence of further peri-implant breakdown, the need for rescue therapy and implant removal was observed in retrospective and prospective studies. To the present date, inconclusive evidence exists to support a gold standard protocol for an effective surgical implant detoxification.

Keywords (MeSH) · Dental implants · Peri-implantitis · Inflammation · Disease management

Introduction

Peri-implant diseases are becoming an imminent problem in modern dentistry. The widespread use of dental implants has led to an alarming increase in the prevalence of peri-implant mucositis and peri-implantitis conditions [1–4]. Recent reports estimate that approximately 1 out of 3 patients and 1 out of 5 implants will experience peri-implantitis [5, 6]. Hence, it is of paramount importance for clinicians performing implant-related procedures to receive a proper training for the diagnosis, prevention, and especially, management of peri-implant diseases.

A clear understanding of the pathogenesis of peri-implant diseases may provide key aspects for the decision-making process on their management. Recent literature reflects the level of diagnostic and therapeutic complexity and multifactorial effect of conditions associated with peri-implant diseases. Based on these observations, treatment of peri-implant diseases might be considered a real challenge. Surgical outcomes of peri-implantitis-affected implants remain unpredictable in arresting inflammation but effective in preventing further bone destruction and implant loss [7•, 8•]. To this date, there is inconclusive evidence available to support a gold standard protocol for an effective surgical implant detoxification [9•].

The purpose of the present article is to provide a narrative review of current protocols (2015–present) used for the treatment of peri-implantitis.

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Pre-surgical Protocols

The majority of prospective human trials have included pre-surgical hygiene programs prior to treatment of peri-implantitis by means of supragingival mechanical instrumentation (e.g., curettes, ultrasonic devices, rubber cups with polishing paste) [10–13], non-surgical therapy with/without local anesthesia [14–16], antimicrobial rinses/gels (e.g., chlorhexidine [CHX] 0.12%) [17–19], and/or locally delivery antibiotics (LDA) (e.g., minocycline) [20]. Additionally, patient education, reinforcement of oral hygiene instructions, and motivational therapies were provided during pre-surgical appointments [10, 11, 21].

Some studies asserted the importance of periodontal stability and their suspicion of the deleterious effect upon treatment of peri-implantitis [13, 22]. Froum and coworkers established in their protocol that all periodontal treatment should be completed at least 1 month prior to treatment of peri-implantitis lesions [22]. Conversely, Stein et al. treated both peri-implant and periodontal conditions simultaneously with antibiotic therapy [13]. Moreover, some authors recommended performing a re-evaluation in an attempt to reassess patient compliance, bleeding, and plaque scores (full-mouth bleeding scores [FMBS]/ full-mouth plaque scores [FMPS] = < 1 or plaque index [PlI]/bleeding index [BI] = < 20%) before proceeding with any surgical intervention [12, 15]. Interestingly, some authors prescribed antibiotic therapy as pre-medication [18, 20], while implant prosthesis removal was advocated by others to facilitate access and mechanical instrumentation and access for regenerative therapy [10, 11, 14, 17–21, 23–25].

It is important to note that these pre-surgical protocols were not advocated to treat peri-implantitis lesions with non-surgical therapy but rather to remove local contributing factors. Hence, a reduction in signs of inflammation and microbial load around implant sites, and favorable probabilities towards regenerative therapy are more likely to be expected.

Methods for Mechanical Detoxification

Regardless of the surgical approach, there is limited evidence to support the best mechanical (e.g., titanium, plastic, carbon, stainless steel curettes) or device-assisted (ultrasonic scalers with metal/plastic tips, air-abrasive devices) method for implant detoxification. The effectiveness of these instruments/devices will be impaired when mechanical instrumentation is performed on exposed implant-threaded surfaces. Often, titanium curettes and ultrasonic devices (with metal or plastic tips) are the instruments of choice for mechanical debridement around peri-implantitis affected implants [10, 12–14, 17–19, 23, 24, 26–31].

Additionally, titanium brushes have been advocated to overcome the limitations of exposed threaded-implant surfaces [12, 17, 19, 26, 28]. Sarmiento et al. proposed to use them on contaminated implant surfaces for 60 s [20]. Cha et al. studied the efficacy of titanium brushes at an oscillating low speed of 900 rpm upon the clinical and radiographic outcomes of treated peri-implantitis sites [26]. After 12 months, it was reported that titanium-brush-treated sites display a reduction in 79% and 55% of probing depths (PD) and bleeding on probing (BOP) respectively. Overall, a successful treatment was noted in 66.7% when compared to non-treated sites (23.1%).

A particular interest in glycine, erythritol, or sodium bicarbonate powders for air-abrasive devices as adjuncts to mechanical debridement were observed in recent publications [13, 19, 22, 26, 28, 32, 33]; however, their efficacy within surgical interventions remains scarce. Parma-Benfenati and coworkers experimented using both glycine and sodium bicarbonate, separately, within the same peri-implantitis site for 1 min during regeneration therapy and reported promising results [28]. Interestingly, some studies used air-abrasive devices in non-surgical approaches for the treatment of peri-implantitis. John and colleagues concluded air-abrasive devices as a monotherapy can significantly reduce PD and BOP scores [32]. Similarly, Stein et al. tested the usefulness of submucosal flexible plastic tips (Perio-flow Nozzle™) for better subgingival access [13].

Other authors have expressed their concerns about the impact of mechanical instrumentation upon implant surfaces and how it might contribute to future biofilm deposition. In such sense, mechanical debridement is limited around the dental implant but not the implant itself and the use dry saline-soaked cotton gauze or pellets as a more conservative approach “to avoid changes on implant surface roughness”. [16•, 24, 29, 30].

Methods for Chemical Detoxification

Chemical agents are commonly used for the treatment of peri-implantitis and considered an integral component of implant decontamination protocols. Among them, hydrogen peroxide [17–20, 27], phosphoric acid [34, 35], and ethylenediaminetetraacetic acid (EDTA) [15, 30] were frequently implemented within surgical interventions, with hydrogen peroxide being the most consistent chemical agent used in human studies. Interestingly, experimental in vitro models evaluating sodium hypochlorite (NaOCl) [36–40] and citric acid [41] for chemical implant detoxification revealed positive effects; however, human-controlled studies were not found in recent literature. Sarmiento et al. described using a 0.9% NaOCl solution intended to remove residual hydrogen peroxide [20].

Limited studies with promising results had introduced new adjunct chemicals within a non-surgical approach for peri-implantitis. Pini-Prato et al. experimented with a mixture solution composed of hydrobenzenes, sulfonate group, and sulfuric acid due to their keratolytic, hygroscopic, and denaturing properties [42]. All treated sites showed significant reduction

of PD and BOP after 3 and 6 months of treatment with only a moderate transient discomfort that disappeared after a 2- or 3-day post-treatment.

On the other hand, Roos-Jansåker and colleagues explored the effects of chloramine, a product of 0.95% NaOCl and specific amino acids (leucine, lysine, and glutamic acid), as an oxidant agent to disrupt biofilm and remove granulation tissue as an adjunct to non-surgical therapy [23]. The chemical was applied in the peri-implant pocket prior, during and after mechanical detoxification. Unresponsive sites were subject to rescue therapy 6 weeks and 3 months as needed. Nonetheless, the addition of this chemical was equally effective in the reduction of inflammation compared to conventional mechanical detoxification after 3 months. Table 1 contains a summary of application methods for accepted chemical agents used in treating peri-implantitis.

Kotsakis and coworkers reported multiple chemical agents (20% citric acid, 24% EDTA, 1.5% NaOCl) can produce elemental contaminants that might alter the titanium physiochemistry [37]. Despite their positive antimicrobial effect, chemical residues can induce a cytotoxic effect and adversely affect the cellular response to decontaminated surfaces. Findings from this study reflected the importance of implant surface properties as a modulating factor other than bacterial biofilm for the outcomes after surgical treatment of peri-implant diseases.

Table 1 Application methods of chemical agents

Chemical agent	Methodology
Hydrogen peroxide	Concentrations: 3% (most common) and 5% Application: cotton pellet soaked with chemical solution Working time: 1 min
EDTA	Concentration: 24% Application: Apply gel on dried implant surface Working time: 2 min
Citric acid	Concentration: 20% Application: cotton pellet soaked with chemical solution Working time: 30 s to 1 min
Phosphoric acid	Concentration: 35–37% Application: apply gel on dried implant surface Working time: 1 min
NaOCl	Concentration: 0.1–1.3% Application: cotton pellet soaked with chemical solution Working time: 30 s to 1 min
Chloramine	Concentration: 0.95% NaOCl and amino acid solution Application: apply gel before, during and after mechanical instrumentation. If needed, reapplication after 6 weeks and 3 months Working time: 30 s

Surgical Protocols for Peri-implantitis

Modest and unpredictable outcomes are usually expected from non-surgical interventions for peri-implantitis lesions [43]. Surgical approaches for the treatment of peri-implantitis are often selected for better access to implant detoxification. The decision-making process to choose an ideal intervention to treat peri-implantitis was previously proposed [44]. Only current surgical protocols and innovative approaches (2015–present) are discussed in the following sections.

Open Flap Debridement

Hallström and colleagues acknowledged how surgical resective and/or regenerative procedures might have shown promising outcomes for the treatment of peri-implantitis; however, an open flap debridement (OFD) was selected to explore only the effects of antibiotic therapy as an adjunct to treatment of peri-implantitis [29]. Following intrasulcular incisions and a muco-periosteal flap, mechanical instrumentation was performed with hand curettes and saline-soaked gauze with or without antibiotic therapy. It was concluded that OFD without antibiotic therapy is effective in approximately 25% of the cases after 12 months of treatment using a very strict success criterion. Conversely, Renvert at al. reported less successful outcomes (5%) with OFD when compared to regenerative therapy [27].

Apically Positioned Flap

Dental implants with < 2 mm of keratinized mucosa (KM) are more likely to be associated with peri-implant disease during supportive maintenance therapy [45]. Thus, preservation of KM is a key factor to consider when performing surgical interventions around peri-implantitis affected implants [20, 21]. Sarmiento et al. performed an apically positioned flap (APF) in combination with mechanical (ultrasonic and titanium curettes) and chemical (5% hydrogen peroxide and 0.9% sodium chloride) detoxification along with laser therapy (Er:YAG) [20]. Reductions in PD (6.79 mm to 4.32 mm) and BOP (100% to 14.3%) were reported after a 6-month post-operative.

Resective Therapy

Resective approaches (e.g., osseous, implantoplasty) are usually considered around implants with suprabony defects (SBD) or infrabony defects (IBD) not suitable for regenerative therapy [8, 18, 20, 25•]. Short-term results have shown resective procedures to be effective for reductions in PD (5.86 to 3.63 mm) and BOP (100% to 0%) [20]. Conversely, Koldsland et al. found that the effect of treatment is reduced

when suppuration and bone loss exceeding 7 mm are present prior to intervention [18].

Long-term human studies have revealed more realistic outcomes for these surgical methods and provided valuable information upon the behavior of treated peri-implantitis lesions. Carcuac and coworkers used bone recontouring techniques to treat peri-implantitis sites with different anti-infective protocols [8]. Successful outcomes were obtained in 45% of all implants and were highly correlated to implant surfaces characteristics. Non-modified implants (79%) displayed better outcomes than those with modified surfaces (34%) after 1 year. Three-year post-operative outcomes revealed stable bone levels (mean 0.04 mm) and an average reduction in PD of 2.7 mm and inflammation signs (BOP and suppuration) by 40%.

Similarly, Berglundh, Wennström, and Lindhe demonstrated long-term outcomes using their trademark methodology in a 2–11-year retrospective study [25•]. When indicated, osseous recontouring is performed to facilitate pocket elimination followed by mechanical detoxification with titanium curettes and saline-soaked gauze. Marked reduction in post-surgical PD and BOP and stable bone levels were observed during the observation period. Similarly to Carcuac et al., they also noted that non-modified implant surfaces (e.g., turned) responded more favorable to therapy than modified surfaces (e.g., TiUnite, TiOblast, Osseospeed, titanium plasma spray [TPS], sandblasted large-grit, and acid-etched [SLA]).

On the other hand, implantoplasty has been indicated as a method to remove exposed threads of SBD and eliminate niches for further biofilm deposition [16•, 17, 21]. Removal of implant threads is performed with diamond burs of 40 μm and 15 μm grit sizes, whereas Arkansas stones and rubber flame-shaped burs are considered for polishing purposes. A case series of 25 patients with 40 implants, Englezos et al. demonstrated high survival rates (100%), significant PD reduction (8.7 mm to 3.3 mm), and a mean of 2.5 mm of recession and stable bone levels after 2 years [20]. Nonetheless, only 67.5% of the implants showed PD ≤ 4 mm, 25% still displayed BOP, and therapy was less effective with plaque scores > 40%. Patient-related outcomes should be highly considered when performing resective procedures since esthetics will be highly compromised.

In certain occasions, combination therapy (implantoplasty and GBR) might be indicated at sites with both SBD and IBD. Schwarz, John, and Becker observed clinically important defect resolutions at surgical reentries using this approach when treating buccal bony dehiscence with a semicircular component [46]. Furthermore, a 7-year follow-up study by the same group revealed effective outcomes regardless of the method of surface decontamination (e.g., Er:YAG laser or plastic curettes/saline-soaked cotton pellets) for the IBD component [16•].

Regeneration Therapy

A myriad of studies have explored the potential for guided bone regeneration (GBR) within peri-implantitis affected sites [12, 14–17, 19, 20, 22, 27, 28, 30•, 47•]. The addition of different bone substitutes (e.g., autograft, allografts, xenografts, alloplasts) with or without barrier membranes (e.g., absorbable, non-absorbable) as adjuncts to the surgical treatment of peri-implantitis have demonstrated promising results.

Bovine-derived xenograft has been the preferred choice of material by many clinicians for the treatment of peri-implantitis defects [12, 14–16, 20, 30•, 47•, 48]. Renvert et al. demonstrated that regenerative therapy (xenograft only) of well-contained IBD was effective in 42.9% of cases [27]. Moreover, the absence of BOP (47.6% of patients) and a higher radiographic defect fill were noted compared to OFD after 1 year. Similarly, Mercado and colleagues noted a 56.6% treatment success after 3 years when combining xenograft with a biological agent (enamel matrix derivatives [EMD]) and doxycycline solution [30•].

Roccuzzo et al. reported treatment success rates of 52.1% with a significant decrease in BOP (71.5% to 18.5%) using xenograft and connective tissue grafts (CTG) [15]. Despite the promising outcomes, complete resolution of the pathological lesion was not predictable and decisions for treatment should be driven by patient-related elements. A 7-year follow-up by the same group reported that the implant surface characteristics played a role in both survival and success rates of peri-implantitis-treated implants [47•]. It was noted that SLA implants respond more favorably than TPS implants (58.3% vs. 14.3%). Furthermore, rescue treatment was considered in 8 out of 26 implants by means of a new surgical intervention and additional antibiotic therapy with 4 of them later lost due to biological complications.

On the other hand, absorbable (e.g., collagen-derived) as well as non-resorbable (e.g., dense- or expanded-polytetrafluoroethylene [d-PTFE or e-PTFE]) membranes have been incorporated to GBR around implants as a cell-occlusive barrier [12, 14, 16•, 17, 19, 20, 22, 28]. Scarce literature was found on GBR performed with PFTE membranes. Parma-Benfenati et al. reported the potential of e-PTFE membranes for submerged approaches, with a defect bone fill ranging between 50 and 100% [28]. Experienced clinicians display concerns for a new surgical intervention to recover membranes that are usually associated with a surgically induced soft tissue recession.

Isler and colleagues reported that regeneration therapy (xenograft and a collagen membrane) for peri-implant IBD yielded a significant reduction in the gingival index (GI), BOP, PD, clinical attachment level (CAL), and vertical defect fill of 1.99 mm after a 12-month post-operative [14]. Moreover, Sarmiento et al. reported GBR procedures with a biologic agent (e.g., platelet-derived growth factor [PDGF])

and a collagen membrane can significantly reduce PD (7.21 mm to 4.09 mm) and BOP (100% to 10.6%) after 6 months [20]. Interestingly, they performed an internal decortication of the IBD prior to adding the regenerative biomaterials. Furthermore, Schwarz and coworkers concluded treatment outcomes were not influenced by decontamination methods, but rather the peri-implant defect morphology [16•].

Long-term studies have shown GBR procedures might deteriorate over time. La Monaca and coworkers reported high success rates (91%) within 1 year of treatment; yet, the 5-year outcomes revealed that these were not sustained as success rates decreased to 59% [19]. In a 10-year case series of 170 implants, Froum and colleagues experimented with different treatment alternatives for peri-implantitis and reported survival rates of 98.8% [22]. GBR was performed with bone allograft, absorbable membrane, and in some occasions, CTGs as a multi-layer approach. Overall, BOP was eliminated in 91% of all included implants and signs of bone gain (1.77 mm) and soft tissue gain (0.52%) were observed. Nonetheless, 18 implants required a new surgical intervention while 10 of them were subject for a third procedure.

Other bone substitute materials might also be considered within GBR procedures. De Tapia reported radiographic bone fill of 84% and successful treatment in 66.7% of cases by using a mixture of calcium phosphate and hydroxyapatite [17]. Guler and colleagues demonstrated comparable results using porous titanium-derived granules as a new bone substitute in terms of CAL values (5.29 mm to 3.59 mm) and radiographic bone fill (4.77 mm to 3.30 mm) compared to GBR with xenografts, collagen membrane, and blood-derived membranes (e.g., platelet-rich fibrin [PRF]) [12].

Ultimately, available evidence on regenerative therapy for peri-implantitis is limited and inconclusive due to scarce controlled studies, high heterogeneity between studies, and incomparable treatment outcomes [49••].

Adjunct Therapy

Biologic Agents

Within implant dentistry, biologic agents are adjuncts meant to promote both soft and hard tissue regeneration around peri-implantitis sites. Among recent studies, the effects of EMD [22, 24, 30•, 50•] and PDGF [20, 22, 51] revealed promising results. Seemingly, better marginal bone levels and microbial profiles associated with more gram-positive bacteria were encountered after OFD with EMD [24]. Moreover, long-term implant survival is enhanced when compared to non-EMD treated sites after 3 and 5 years [50•]. Future randomized clinical trials should emphasize the individual effect of these biologic agents prior to advocating their use in the treatment of peri-implantitis [30•].

Antibacterial Mouth Rinses

The addition of antibacterial mouth rinses (e.g., CHX, cetylpyridinium [CPC]) as a pre-surgical, intraoperative, and post-surgical adjunct has been extensively described [10, 11, 17–20, 22]. CHX is the most commonly applied agent during the treatment of peri-implantitis. Concentrations of 0.12% and 2% have been tested by rinsing the surgical area up to 60 s and immediately followed by a saline rinse of 1 min [19, 20, 22]. It has been consistently reported that CHX does not improve clinical or radiographic treatment outcomes when used as an adjunct [10, 11]. However, a significant reduction in the anaerobic microbial load was reported after 12 months of resective treatment [11].

On the other hand, the antimicrobial effect of CPC has been shown to inhibit bacterial growth related to peri-implant diseases [52••, 53] and reduce bacterial load during surgical treatment of peri-implantitis [11]. Additionally, a repeated submucosal delivery of povidone-iodine (POV) solution has been proposed as a novel non-invasive therapy for peri-implantitis. Stein and colleagues promoted the slow release of POV for 10 s repeated three times per implant site with an additional application after 7 days [13].

Systemic and Locally Delivered Antibiotics (LDA)

The significance of antibiotic therapy as an essential component of surgical peri-implant therapy remains debatable. Systemic antibiotics, such as azithromycin [27, 29, 54–56], amoxicillin [10, 12, 14, 17, 19, 21, 26, 28], clindamycin [20], and metronidazole [14, 17, 19], used as adjuncts have revealed higher treatment success (46.7% vs. 25.0%) [29] and a reduced number of PD > 4 mm [13].

It was reported that modified implant surfaces tend to respond less favorable to treatment than non-modified when associated with antibiotic therapy [10]. Overall, the addition of antibiotics failed to provide a sustained benefit in terms of BOP, PD, radiographic bone loss, and microbial load after 1 year of treatment [8•, 13, 29].

In the recent years, the application of LDAs (e.g., minocycline, tetracycline) has been extensively explored and also proposed as potential adjuncts in the treatment of peri-implantitis [19, 20, 22, 26, 28, 57]. However, they are also subject to the same limitations noted with systemic antibiotics. A short-term randomized controlled trial (RCT) by Cha et al. reported that locally delivered minocycline effectively reduced PDs, increased success rates (66.7% vs. 36.63%), and found no traces of *Porphyromonas gingivalis* and *Tanerella forsythia* after 6 months [26]. Table 2 depicts available LDAs used for peri-implant diseases.

Table 2 LDAs used for the treatment of peri-implantitis

LDA	Method of application
Minocycline 2% (10 mg in 0.5 g ointment)	Intraoperatively: apply even layer upon implant surface Post-surgically: repeated non-surgical application at 1–2 weeks, 1 and 3 months
Tetracycline 50 mg/mL	Intraoperatively: apply for 3 min and rinse with saline solution from 30 to 60 s

Blood-derived Concentrates

The rationales for the incorporation of blood-derived concentrates (e.g., PRP, PRF) as adjuncts in regenerative therapy are aimed at accelerating angiogenesis, stimulating osteoblast/fibroblast activity, and enhancing tissue regeneration [58]. Limited clinical studies have explored the use of blood-derived concentrates as barrier membranes or filler materials for the treatment of peri-implantitis [12, 14]. Guler used PRF as a barrier membrane to cover defects filled with porous titanium granules [12]. Authors then speculated that PRF membranes could prevent granules migrate into the periosteal flap; however, the clinical outcomes of this approach remains unclear. Furthermore, Isler and colleagues used concentrated growth factors (CGF), obtained from centrifuged venous blood, for the treatment of peri-implantitis [14]. After implant detoxification, a bovine-derived xenograft was applied to fill the IBD and then covered with either collagen or double-layer CGF membrane. Despite yielding significant improvements in regard to radiographic defect fill, GI, BOP, PD, CAL, and mucosal recession, results were in favor of GBR procedures at a 12-month post-operatively.

Lasers

Modern dentistry is embracing the employment of lasers in a variety of surgical approaches. The effects of lasers are dependent upon the energy emitted by the device and ability of the targeted tissue to absorb, scatter, reflect, or transmit this energy. Carbon dioxide, Nd:YAG, Er:YAG, Er,Cr:YSGG, and diode lasers are types of lasers available for periodontal and peri-implant procedures [59].

Nowadays, laser therapy is being commonly used as an adjunct to non-surgical [31, 60, 61] and surgical procedures [16•, 20, 51]. Ideal settings are dependent on the manufacturer's recommendations. A recent meta-analysis by the AAP best evidence consensus concluded that laser therapy (limited to Er:YAG, carbon dioxide, and diode lasers) can provide minimal benefits in PD reduction, CAL gain, recession improvement, and Pl scores in the treatment of peri-implant diseases [62••].

Antimicrobial Photodynamic Therapy (aPDT)

The exposure of photosensitizers (e.g., phenothiazine chloride, tolonium chloride, indocyanine green dye, methylene blue dye, toluidine blue dye) to low-intensity diode lasers will purposely aim for the formation of free radicals meant to behave as toxic agents against periodontal pathogens. Emerging evidence continues supporting the use of antimicrobial photodynamic therapy (aPDT) as an adjunct during treatment of peri-implant diseases [28, 63–66]. However, this is contradictory with current AAP best evidence consensus which concluded that aPDT provides similar clinical outcomes compared to conventional therapy for the treatment of both periodontitis and peri-implantitis [67••]. The advantages of aPDT might be beneficial during active application of photosensitizers and remain effective for short terms after aPDT is discontinued.

Soft Tissue Augmentation

The presence of < 2 mm-keratinized mucosa constitutes a site-specific risk factor for peri-implant diseases for erratic maintenance compliers [45]. Thus, soft tissue augmentation around dental implants should be considered more often for site development prior to or after implant placement. No available RCTs were found evaluating the individual effect of free soft tissue graft (e.g., connective tissue graft [CTG], free gingival graft [FGG]) or substitutes (e.g., acellular dermal matrix [ADM]) for the treatment of peri-implantitis. Limited studies have included in their surgical protocol the addition of a soft tissue graft to ensure the stability of the grafting material or when limited keratinized mucosa was present [15, 22, 30•, 35].

Innovations

Probiotics

In recent years, probiotics are emerging as an innovative approach to prevent and improve systemic and oral conditions. Two studies have explored the influence of *Lactobacillus reuteri* as adjuncts limited to non-surgical treatment of peri-implantitis lesions [56, 68]. Galofre et al. tested a daily use of probiotics in the form of lozenges containing a combination of 2 strains of *L. reuteri* (PerioBalance®, Sunstart Suisse SA) for 30 days and a maximum follow-up of 90 days [68]. A significant 3-fold decrease in BOP that remained stable for the length of the study was reported. However, a very limited effect was noted on the peri-implant microbiota. Such findings were confirmed by Tada et al. after evaluating the effects of *L. reuteri* for 6 months [56].

Definition of Treatment Success

As established by Heitz-Mayfield and Mombelli, the definition of success after treatment of peri-implantitis is determined by the presence of ≤ 5 mm PD, the absence of BOP/suppuration, and no progressive bone loss [69••]. Using this strict criterion, up to 50% success rates have been reported in the literature [7, 14, 25•, 26, 47•, 50•, 70•]. In regard to regenerative therapy, radiographic defect fill of > 1 mm or ≥ 25% might be considered as treatment success [27, 71•]. Additionally, the amount of mucosal recession (≤ 0.5 for anterior and ≤ 1.5 mm for posterior) has been taken into consideration to define successful outcomes [30•]. In spite of unpredictable outcomes, some authors have proposed less strict and flexible criteria, based on the number of BOP sites [27, 72].

Conclusions

Based on the current evidence provided, peri-implantitis therapy remains an unpredictable approach to arrest inflammation but effective to prevent further bone destruction and implant loss. To the present date, we still lack conclusive evidence to determine a gold standard protocol for implant detoxification and an effective approach to treat peri-implant diseases. Future studies should keep emphasizing prevention mechanisms until more solid treatment alternatives become available.

Compliance with Ethical Standards

Conflict of Interest Carlos Garaicoa-Pazmino, Khaled Sinjab, and Hom-Lay Wang each declare that they have no conflict of interest.

Human and Animal Rights and Informed Consent This article does not contain any studies with human or animal subjects performed by any of the authors.

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