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Neoadjuvant Treatment Modalities for Peri Implant Diseases

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Abstract

The new era of rehabilitation of partially or complete edentulous patients begins with the introduction of dental implants which have revolutionized the treatment for the last two decades demonstrating high success and survival rates. The functional implants and their restorations may be subjected to mechanical and biological complications.Peri-implant disease is an inflammatory process affecting the surrounding soft and hard tissue around a functional dental implant, which leads to bone loss and loosening of implant.various risk factors and risk indicators influence the pathogenesis of peri-implant disease, among this biofilm plays an important role. Therefore management of peri-implant disease primarily focus on the removal of biofilm. The treatment modality can be nonsurgical management and surgical management. This paper provides an insight into the recent updates on different non surgical approaches to treat peri-implant diseases and to evaluate critically the evidence available to support the different proposed therapies.

Keywords: Peri –implant diseases, Nonsurgical management ,Surgical management.

Introduction

Dental implants have revolutionized the treatment of edentulous patients for the last two decades demonstrating high success and survival rates. However, the long-term success of dental implants is not the same or as high as their survival, as functional implants and their restorations

may be subject to mechanical and biological complications[1].

Peri-implant diseases encompassing two main entities: peri-implant mucositis and peri-implantitis. The 6th European Workshop on Periodontology in 2008, it was proposed that the term ‘‘peri- implant disease’’ is a ‘‘collective term for inflammatory reactions in the tissues surrounding an implant’. Peri-implant mucositis is the presence of inflammation of the periimplant mucosa without sign of loss of bone support, while peri-implantitis, in addition to inflammation of the mucosa, is characterized by a loss of bone support .[2]Different risk factors and risk indicators that may influence the pathogenesis in favor of tissue destruction include poor oral hygiene, patients age, a history of periodontitis ,presence of peridontitis, and cigarette smoking, diabetes, genetic traits, the implant surface or the lack of keratinized mucosa, alcohol consumption and implant related complication .Approximately 65% of all infectious diseases, including periodontal and periimplant diseases are associated with biofilms .

The management of peri-implant disease primarily focuses on the removal of biofilm . The treatment modality can be divided into (1) Nonsurgical management and (2) Surgical management; surgical management encompass resective and regenerative treatment.In non surgical therapy ,surface debridement constitutes the basic element for treatment .However, the design of the supra structure may hinder effective mechanical treatment of the infected implants. Therefore, adjunctive therapies like antibiotics, antiseptics and laser treatments have been proposed in order to improve the non-surgical treatment options of periimplant mucositis and peri-implantitis. This reviews update different non surgical approaches to treat peri-implant diseases and to evaluate critically the evidence available to support the different proposed therapies.

Peri- implant diseases

Peri-implant diseases encircle two main entities: peri-implant mucositis and peri-implantitis. It is a ‘‘collective term for inflammatory reactions in the tissues surrounding an implant’’.Peri implant mucositis include the signs of inflammation in the periimplant tissues , with no signs of loss of supporting bone. Whereas If the inflammation persists, peri-implant mucositis get progressed into peri-implantitis which is characterized with an profuse bleeding, suppuration , increased probing depths(>6 mm) and progressive bone loss[3]. Today, the prevention as well as early detection of peri-implant mucositis remains as key components in successful dental implantology.It is paramount importance that the identification of both local and systemic factors affecting the incidence and severity of such conditions for the proper management. Ideal management of peri-implant diseases focuses on controlling the infection and arresting progression of bone loss without compromising esthetics and achieving bone regeneration.

Therapeutic strategies for peri implant diseases

Therapeutic strategies for peri implant diseases is divided into three parts: therapy of peri-implant mucositis; nonsurgical therapy of peri-implantitis; and surgical therapy of periimplantitis. The treatment of peri-implant lesions usually includes mechanical debridement of biofilm and calculus. This therapy may be rendered through professional intervention or by the patient using home-use oral-hygiene techniques. In addition, adjunctive antimicrobials, such as antiseptics, or local or systemic antibiotics, may be used in conjunction with mechanical debridement alone or with mechanical debridement and mechanical plaque-control protocols. But in case of moderate to severe Peri-implantitis a nonsurgical therapy

alone might be sufficient or a step-wise approach with a non-surgical therapy followed by a surgical treatment is necessary. However the non surgical management is critical in maintance of peri implant health as well as arresting the disease progression.

Primary goals of the treatment [4]

• Elimination of peri-implant mucosal inflammation.

• Cessation of peri-implant disease progression.

• Maintenance of functionality of implant with healthy peri-implant tissues.

• Regeneration of lost peri-implant tissues.

• Restoring peri-implant esthetics such as treatment of mucosal recession, inadequate width, and thickness of peri-implant mucosa.

Cumulative interceptive supportive therapy

Depending on the clinical and the radiographic diagnosis, a protocol of therapeutic measures has been designed to head off the development of peri-implant lesions. This protocol is cumulative in nature and includes four steps (supportive therapy protocols A–D).

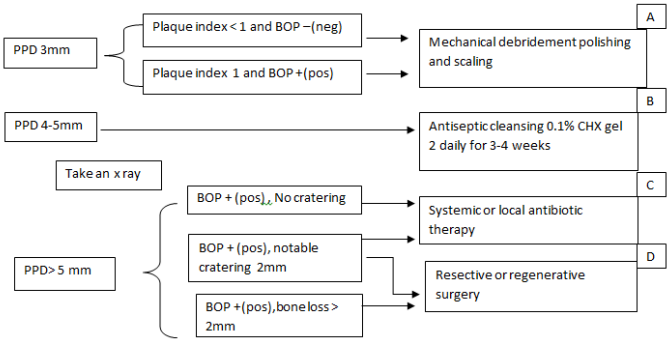

Figure 1:Decision tree for cumulative interceptive supportive therapy(CIST).Depending on the mucosal condition and probing dpth, either regime A or regime A+B, regime A+B+C,or regime A+B+C+D are performed .(A) Mechanical debridement;(B) Antisepticcleansing (C) antibiotic therapy (D) respective or regenerative surgery.

In 2004 the CIST protocol was modified and called AKUT-concept by ***Lang et al 2004*** [5] .The basis of this concept is a regular recall of the implanted patient and repeated assessment of plaque, bleeding, suppuration, pockets and radiological evidence of bone loss.

Table 1: AKUT-protocol by Lang et al. 2004

Stage	Result	Therapy
	Pocket depth (PD) < 3 mm, no plaque or bleeding	No therapy
A	PD < 3 mm, plaque and/ or bleeding on probing	Mechanically cleaning, polishing, oral hygienic instructions.
B	PD 4-5 mm, radiologically no bone loss	Mechanically cleaning, polishing, oral hygienic instructions plus local antiinfective therapy (e.g. CHX)
C	PD > 5 mm, radiologically bone loss < 2 mm	Mechanically cleaning, polishing, microbiological test, local and systemic antiinfective therapy.
D	PD > 5 mm, radiologically bone loss > 2 mm	Resective or regenerative surgery

Non-Surgical Treatment of Peri-Implant Disease

The removal of the plaque and calculus on the implant surface it is necessary to achieve its long-term success . The mechanical procedures to clean the implant should ideally be capable of removing efficiently the bacterial deposits without altering the implant surface, which may negatively affects its biocompatibility.[6]

Roughness on the titanium implant surfaces may alter the response of the surrounding soft tissues, directly influencing on the posterior dental biofilm formation and making difficult its proper removal . On the other hand,

scaling procedures may also alter the oxide layer on the implant surface, which can result in the corrosion increase . Therefore, one should attempt to maintain the integrity of the implant surface and prosthetic components during the scaling procedures . Different instruments have been proposed for the scaling of the implants.[5]

Instruments

Different debridement systems have been evaluated, normally in combination with polishing the implant surface and/or the prosthetic components using a rubber cup and a polishing paste or using an abrasive sodium-carbonate air–powder system. Such debridement systems include curettes and ultrasonic devices with polyether-etherketone-coated tips.

Curettes: Curettes of different materials have been produced for use specifically to debride implant surfaces.[7]

- Steel curettes have an external hardness higher than titanium and accordingly are not indicated for cleaning titanium implants. Nevertheless, they can be used on other implant surfaces, such as titanium zirconoxide or titanium oxinitride .
- Titanium-coated curettes have a similar hardness to the titanium surface and thus do not scratch its surface.
- Carbon-fiber curettes are softer than the implant surface and therefore remove bacterial deposits without damaging the surface, although they break easily .
- Teflon curettes have similar properties to carbonfiber curettes and they have been proposed for use in combination with air-abrasive systems.
- Plastic curettes are the most fragile of all curette types and have limited debriding capacity.

Ultrasonic devices

Similarly to curettes, ultrasonic devices are to remove biofilm and calculus without altering the implant surface. To accomplish this, different tip modifications have been proposed, such as carbon fiber, silicone or plastic. A modification to the conventional ultrasonic device is the Vector- system (Durr Dental, Bietigheim-Bissin- € gen, Germany), in which the horizontal vibration is converted by a resonating ring into a vertical vibration, resulting in a parallel movement of the working tip to the surface.[8]

Table 2: Studies on Clinical efficacy for implant surface debridement

Author and year	Instrumentation	Results
Fox et al. 1990 [9]	Plastic, stainless steel and titanium alloy curettes	Concluded that the surfaces scaled with metallic instruments showed a higher degree of roughness than those not treated and those treated with plastic curettes.
Dmytryk et al.1990 [10]	Plastic, stainless steel and titanium alloy curettes	Reported that after 24 hours, only the surfaces scaled with steel curettes showed a statistically smaller mean of adhered fibroblasts counting than the control group. After 72 hours, the surfaces treated with stainless steel and titanium alloy exhibited a statistically reduction in the number of cells adhered. Morphological alteration in the cells were observed in the group scaled with stainless steel curettes,

McCollum et al. 1992 [11]	A i r abrasion, plastic curette, rubber cup with pumice	Concluded that the methods tested did not alter the titanium surface.
Homiak et al. 1992 [12]	Metallic and plastic curettes, rubber cup, rubber cup with tin oxide, air abrasion	Reported that metallic curette increased the titanium surface roughness, while the other treatment left a more polished surface, decreasing the previous machine marks
Mengel et al. 2004 [13]	Titanium, steel, and plastic curettes, rubber cups, metallic ultrasonic point and air abrasion	Concluded that steel and titanium curettes and the ultrasonic points led to the removal of the surface coverage and to the increase of the roughness deepness of the implant surfaces. Damages to the surface were not observed after the use of rubber cups, air abrasion and plastic curettes
Baek et al. 2011 [14]	Cooper point, plastic head point and conventional stainless steel point	Demonstrated that the stainless steel point increased the surface roughness. The cooper point caused minimum damages to the titanium surface similar to the results obtained by the two types of plastic points
Mann et al. 2012 [15]	Conventional and plastic modified ultrasonic point	Concluded that metallic ultrasound point caused damages to the titanium surface. The plastic insertion onto the metallic point provided only polishing action, leaving plastic residues on the implant surface
Ji et al. 2014 [16]	Implants were treated using ultrasonic scalers with carbon-fiber tips and conventional method.	Demonstrated that use of ultrasonic scalers with carbon-fiber tips shows better result in terms of pocket depth ,bleeding on probing
Carlo Bertoldi et al 2016 [17]	Changes to titanium implants smooth-surfaces after instrumentation were comparatively analyzed using LV - SEM and WLC profilometry, to accurately evaluate curved surfaces	Concluded that the careful use of titanium-curettes could produce only minimal smooth surface alteration particularly over prolonged treatments, and avoid debris production that could endanger implant preservation.
Benyapha sirinirund et al 2019 [18]	Evaluate topographic changes and effectiveness of mechanical instrumentation(3 curettes:SS Stainless steel,PT Plastic,TI Titanium) on implant surface	Demonstrated that the artificial calculus removal by mechanical instrumentation,with the exception PT:platic curettes,was proven to be clinically effective.All instruments induced minor to major topographic changes upon dental implant surfaces.

[LV -SEM -low-vacuum scanning electron microscopy , WLC -white-light confocal , SS -Stainless steel]

Air Powder Abrasives (Ap) And Rubber Cups Adjuncts To Mechanical Therapy

The use of an abrasive powder, like sodium bicarbonate, sodium hydrocarbonate , or the amino acid glycine , propelled by a stream of compressed air and water is called air powder abrasive. This technique uses pressures of 65 to 100 pounds per square inch (psi) and has been demonstrated with in vitro and in vivo studies to be effective in cleaning the previously contaminated implant surfaces . [19]

Rubber cups, they also have shown to generate significant smoothening of the titanium surface and significantly decrease roughness by removing surface debris and rounding off the sharp machined grooves present on the untreated abutment surface.[7]

Table 3: Studies on air powder abrasives (ap) and rubber cups adjuncts to mechanical therapy.

Author/Study Design	Test	Control	Outcome
Renvert et al 2010 [20]	OHI+ air-abrasive device, glycine powder	OHI+ Er: YAG Laser	Concluded that the results were limited and similar between the two methods compared with those in cases with severe peri-implantitis.
Schwarz F et al 2011 [21]	OHI + air-abrasive device,AAD (amino acid glycine powder)	OHI + mechanical debridement using carbon curets and antiseptic therapy with chlorhexidine digluconate .	Concluded that (i) both treatment procedures resulted in comparable but limited CAL gains at 6 months, and (ii) OHI1 AAD was associated with significantly higher BOP reductions than OHI.
Ji et al 2014 [16]	OHI+ Mechanical debridement (ultrasonic scaler with carbon fibre tips) + air-abrasive device, glycine powder (sites with PD ≥ 4 mm)	OHI+ Mechanical debridement (ultrasonic scaler with carbon fibre tips)	Demonstrated that nonsurgical mechanical therapy alone could effectively control peri-implant mucositis, adjunc tive GPAP treatment had limited beneficial effects compared with mechanical therapy alone.
De Siena et al 2014[22]	OHI+ Mechanical debridement Teflon curets, polishing) + air-abrasive device, glycine powde	OHI+ Mechanical debridement Teflon curets, polishing)	Showed that both techniques were useful for the treatment of peri-implant mucositis. In the test group (with glycine powder), a significant reduction of probing depth was observed.
John et al 2015[23]	OHI+ air-abrasive	OHI+ Mechanical	Demonstrated that (i) both treatment

	device, glycine powder	debridement (carbon curets + 0.1% CHX)	procedures resulted in comparable but limited CAL gains at 6 months, and (ii) OHI+ amino acid glycine powder was associated with significantly higher BOP reductions than OHI+MD.
Lupi et al 2017 [24]	OHI + air abrasive with the glycine powder treatment	Manual debridement and chlorhexidine administration treatment group .	Concluded that treatment with glycine seems appropriate in the maintenance of peri-implant health and more effective than the traditional treatment with plastic curette and chlorhexidine.

[OHI- Oral hygiene instruction, AAD -Amino acid glycine powder, CAL- Clinical attachment level ,BOP- Bleeding on probing,MD- Mechanical debridement, CHX- Chlorhexidine, Er:YAG- erbium-doped yttrium aluminium garnet]

It can be concluded that air powder abrasive can contribute to the detoxification of the implant surface and can produce a surface that is smoother than the original . Negative adverse effects like subcutaneous emphysema and epithelial desquamation have been reported with the use of air abrasive around teeth and around implants . This potential complication may be prevented if the tip if the instrument is used at a 45° angle to the implant .[25]

Rubber cups have shown to generate significant smoothening of the titanium surface and significantly decrease roughness by removing surface debris and rounding off the sharp machined grooves present on the untreated abutment surface . In another in vitro study it was shown that the rubber cup, the plastic curette, and AP left the implant surfaces unchanged . Polishing the implant surfaces with pumice and a rubber cup combined with irrigation with chlorhexidine and systemic antibiotics results in reduction of anaerobic bacteria and bleeding scores in patients with periimplantitis .[7]

Antimicrobial Treatment Adjuncts To Mechanical Therapy

Adjunctive therapies, such as antiseptics and antibiotics, have been proposed to improve the results of nonsurgical debridement as reduction of bacterial loads to levels compatible with tissue health is difficult to accomplish using mechanical means only .[26]

Antiseptic treatment

In addition to performing the mechanical debridement, antiseptic treatment is performed in situations where – in addition to the presence of plaque and BOP – probing depth is increased to 4–6 mm. Suppuration may or may not be present. The antiseptic treatment is performed in conjunction with the mechanical treatment and comprises the application of the most potent antiseptic available [(i.e., chlorhexidine digluconate), either in the form of a daily rinse of 0.1%, 0.12%, or 0.2%, or as a gel applied to the site of desired action . Generally, 3–4 weeks of regular administration are necessary to achieve positive treatment results. Antiseptic rinses with chlorhexidine or applications of chlorhexidine gels may also be recommended for chemical plaque control on a preventive basis. This protocol has been validated both clinically and histologically in an animal experiment and in humans .[7,8]

Table 4: Studies on antiseptic treatment adjuncts to mechanical therapy

Author/Study Design	Intervention	Outcome
Ramberg P, et al 2009 [27]	Control: sodium fluoride toothpaste after a period of home-use of 6 months. Test: triclosan/copolymer-containing toothpaste	Concluded that a higher performance of triclosan/copolymer-containing toothpaste compared with a sodium fluoride toothpaste after a period of home-use of 6 months, in terms of bleeding on probing, despite the fact that no changes were noted among groups for plaque index or probing depth.
Thöne- Mühling et al 2010 [28]	Control: SRP with curettes and ultrasonic.Test: SRP with curettes and ultra sonic one application of 1% CHX gel sub-gingivally 1 minute brushing of the dorsum of the tongue with 1% CHX + 0.2% CHX spray on tonsils once daily for 14 days minute rinse with 0.2% CHX solution for 14 days.	Reported that nonsurgical treatment of peri – implant mucositis was effective with or without CHX. Addition of CHX did not display any significant differ
Grusovin MG et al 2010 [29]	Control: chlorhexidine irrigation Test: chlorhexidine mouthrinse.	Reported that superior results of chlorhexidine irrigation, compared with chlorhexidine mouthrinse, in reducing plaque and marginal bleeding
Heitz-Mayfield et al 2011 [30]	Control: One-time debridement with curettes and polishing pastes OHI twice a day (for 4 weeks). Test:One-time debridement with curettes and polish ing pastes + OHI twice a day with 0.5% CHX gel around implant (for 4 weeks).	Concluded that nonsurgical treatment and oral hygiene was effective with and without adjunct CHX gel, while successful therapy did not always result in complete resolution of the inflammation
Baffone W,et al 2011 [31]	Control: chlorhexidine digluconate (CHX) Test : commonly used mouthrinses	Concluded that 0.2% chlorhexidine, essential oils, stannous fluoride and hexetidine associated with methylparaben and propylparaben were effective in reducing peri-implant biofilm *in vitro*. Among the antimicrobials evaluated, chlorhexidine and essential oils proved most effective in reducing biofilm under experimental conditions.

De Siena et al 2014 [22]	Control:Mechanical therapy OHI + 0.2% CHX mouth wash twice daily for 10 days. Test:Mechanical therapy OHI 0.1% CHX gel for self-administration in pockets twice daily for 10 days.	Demonstrated that both treatments were equally effective. Patients preferred gel over mouthwash, even though it was more difficult to use
Hallström et al 2017 [32]	Test: OHI mechanical debridement (titanium curettes and rubber cup) once a day brushing with a full brush of placebo gel for 12 weeks. Test: OHI mechanical debridement (titanium curettes and rubber cup) once a day brushing with a full brush 0.2% CHX gel for 12 weeks.	Reported that oral care brush-on gel (0.2% CHX) can be a beneficial adjunct to mechanical debridement.
Roos-Jansaker AM, et al 2017 [33]	Test and control. Both implants received supra- and submucosal debridement by ultrasonic instrumentation supplemented with hand instruments. Test group : first received local applications of a chloramine gel (PerisolvTM; RLS Global AB, Gothenburg, Sweden) followed by mechanical instrumentation.	Concluded that non-surgical mechanical debridement with adjunctive use of a chloramine is equally effective in the reduction of mucosal inflammation as conventional non-surgical mechanical debridement up to 3 months
Alberto Pulcini et al 2019 [34]	Control:evaluate the efficacy of a 0.03% chlorhexidine Test:0.05% cetylpyridinium chloride mouth rinse, as an adjunct to professionally and patient-administered mechanical plaque removal,	concluded that mouth rinse demonstrated some adjunctive benefits in the treatment of PiM. Complete disease resolution could not be achieved in every case
Bernal Stewart et al 2020 [35]	Test: toothpaste containing 0.3% triclosan + 2.0% PVM/MA copolymer + 1450 ppm fluoride. Control: toothpaste containing	A toothpaste containing 0.3% triclosan was more effective than a regular fluoride toothpaste in improving the periodontal clinical condition around natural teeth of periodontally healthy

	1450 ppm fluoride.	subjects that have been treated for peri-implantitis and were enrolled in a regular maintenance program for 2 years.

[SRP- scaling and root planning, PVM/MA- Polyvinyl methyl ether/maleic acid,PiM- ***Peri-implant mucositis*** , OHI- Oral hygiene instruction,CHX- Chlorhexidine]

Local and systemic antibiotics adjuvant to mechanical therapy

The pocket with increased depth represents an ecological niche which is conducive to colonization with Gram-negative anaerobic periodontopathic microorganisms.The antibacterial treatment approach must then include antibiotics to eliminate or at least significantly reduce the pathogens in this submucosal ecosystem. Prior to administering antibiotics, the mechanical and the antiseptic treatment protocols have to be applied. These therapeutic steps have been validated in a clinical study in which peri-implant infections were treated successfully and remained stable for a documented period of one year. Subsequently, prophylactic procedures were instituted to prevent reinfection.[36]

As an alternative to administration of systemic antibiotics, the application of local antibiotics through the use of controlled delivery devices has emerged as a suitable treatment concept. However, only release devices with adequate release kinetics may be used to assure successful clinical outcomes. The antibiotic must remain at the site of action for at least 7–10 days in a concentration high enough to penetrate the submucosal biofilm. Hence, it appears that peri-implant infections may be controlled successfully by cumulatively providing mechanical, antiseptic, and antibiotic supportive therapy.[7]

Table 5: Studies on Local and Systemic Antibiotics Adjuvant to Mechanical Therapy

Author / Year /Type of Study	Treatment	Outcome
Mombelli & Lang 199[36]	Calculus removal + polishing with pumice and rubber cup+pocket irrigation with 0.5%chlorhexidine + systemic antibiotics (ornidazole; 1000mg, once daily ,for 10days)	Demonstrated that antimicrobial treatment of peri-implant infections, reducing the subgingival bacterial mass and suppressing the anaerobic segment.
Buchmann et al 1996[37]	Intensive hygiene program + occlusal adjustment + scaling + betadine irrigation+systemic antibiotics amoxicillin / clavulanic acid (500mg,three times daily, for 7 days), ormetronidazole(250mg, three times daily, for 7 days)	Concluded that, systemic antibiotics adjunct to the mechanical therapy shows much reduction in the BOP,PD,GI,PI.
Mombelli et al. 2001[38]	Mechanical debridement+tetracycline fibers for 10days	Concluded that, therapy of peri-implantitis by local delivery of tetracycline had a positive effect on clinical and microbiological parameters.

Khoury& Buchmann 2001[39]	Removal of prosthesis + irrigation with 0.2% chlorhexidine + implant scaling + systemic antibiotics (amoxicillin, metronidazole, tetracycline, clindamycin, erythromycin or ciprofloxacin, following antibiotic susceptibility testing)	Concluded that the systemic antibiotics application along with the mechanical therapy improved the basic parameters such as PD,BOP,PI GI,bone loss.
Renvert et al. 2006 [40]	Compare application of minocycline microspheres as an adjunct to mechanical treatment of incipient peri-implant infections with an adjunctive treatment using 1% chlorhexidine gel application.	Concluded that mean probing reductioninthe minocycline group is significantly greater than that in the chlorhexidine group (P<0.001) Reduction in bleeding at the deepest site was significantly greater for the minocycline group compared with the chlorhexidine control(P<0.05)
Salvi et al 2007 [41]	Oral hygiene instruction + mechanical debridement (carbon-fibercurettes)+ 0.2%chlorhexidine gel + minocycline HCl microspheres(Arestin)	Concluded that non-surgical mechanical treatment of peri-implantitis lesions with adjunctive local delivery of microencapsulated minocycline led to positive effects on clinical parameters up to 12 months.
Machteiet al. 2012[42]	a.Mechanical therapy+matrix chips b.Mechanical therapy + chlorhexidine chips	Demonstrated that mechanical therapy and frequent placement of matrix chips and chlorhexidine chips resulted in an improvement in sites with periimplantitis
Sch€ar et al. 2013 [43]	a.Mechanical therapy +local drug delivery (minocycline microspheres) b.Mechanical therapy+photodynamic therapy	Concluded that both the treatments are equally effective in the reduction of mucosal inflammation.
Bassetti et al. 2014 [44]	a..Mechanical therapy + local drug delivery (minocycline microspheres) b.Mechanical therapy + photo dynamic therapy	Concluded that both the treatments are Equally effective inthe reduction of mucosal inflammation.
Faramarzi M et al 2015 [45]	a:Mechanical debridement (MD) alone b: MD in combination with the application of enamel matrix derivative (EMD) and sustained-release micro-spherical minocycline (MSM).	Reported that the use of MSM and EMD can be an adjunctive treatment for management of PIMI and improves clinical parameters and reduces *P. gingivalis* burden three months after treatment.

Kashe fimehr A et al 2017 [46]	a:Mechanical debridement (MD) alone b: MD in combination with the application of enamel matrix derivative (EMD) .	Demonstrated that three-month post-interventional assay revealed significant improvements in BOP and PD in the test group in comparison to the control group ($P < 0.0001$). Relative to control, IL-6 and IL-17 levels were reduced significantly ($p < 0.05$) in the test group compared to the control group.
Alfredo De Rosa et al 2019 [47]	A : the formulation of a controlled-release material containing metronidazole and doxycycline; b, an in vitro evaluation of its antibacterial properties against planktonic and biofilm species involved in periodontal and peri-implant diseases.	The *in vitro* efficacy of the newly formulated gel was confirmed both on planktonic species and on bacterial biofilm over a period of 13 days. The controlled-release gel containing metronidazole and doxycycline had an optimal final viscosity and mucoadhesive properties. It can be argued that its employment could be useful for the treatment of periodontal and peri-implant diseases, where conventional therapy seems not successful.

[MD -Mechanical debridement , EMD-Enamel matrix derivative , MSM-Micro-spherical minocycline , PIMI-Peri implantitis]

Laser and photodynamic therapyadjuvant to mechanical therapy

Laser

By means of a bactericide mode of action, CO2, Diode-, Er:YAG- (erbium-doped: yttrium-aluminum-garnet) and Er,Cr:YSGG- (erbium, chromium-doped: yttriumscandium-gallium-garnet) lasers are used in the treatment of peri-implant diseases with increasing frequency. Minimal absorption and reverberations must be ensured with the purpose to protect implant and tissue. 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 can't be re-induced .Treatment with a CO2 308 nm excimer laser, however, led mainly and efficiently to satisfactory results in an anaerobic bacteria spectrum . In comparison to mechanical methods (plastic curettes), treatments with an Er:YAG laser led to significantly better results in terms of bleeding at peri-implantitis. However, both methods showed no significant differences in changes of pocket depths, clinical attachment level, plaque index and gingival recessions, although in both groups these parameters were improved.[48]However, laser energy at the wrong setting can alter and/or melt the surface of dental implants, potentially interfering with re-osseointegration.

Table 6: Studies on the effect of laser on the treatment of peri implant diseases

Author/ year	Treatment group	Laser Type	Outcome
Renvert et al. 2011[49]	T:Laser C:Air-abrasive	Er:YAG	Demonstrated that clinical improvement was similar between treatments using an Er:YAG laser or air-abrasive for debridement.
Deppe et al. 2013[50]	Air-abrasive+ laser 1:moderate boneloss 2:severebone loss	Diode	Concluded that non-surgical diode laser treatment could stop bone resorption in moderate peri-implant defects but not insevere defects
Arısan et al. 2015 [51]	T:MD+laser C:MD(plastic curets)	Diode	Reported that diode laser did not yield any additional positive influence on the peri-implant healing compared with conventional scaling alone.
Lerario et al. 2016 [52]	T:MD+laser C:MD (ultrasonic scaler and titanium curets)	. Diode	Demonstrated that diode laser seemed to be a valuable tool in the treatment of mucositis and peri-implantitis. Significant PD and BOP reduction was observed
Guo-Hao Lin et al 2018 [53]	T: lasers+ OHI C:OHI	Er:YAG, CO2, and diode lasers.	Concluded that lasers when used as an adjunct to non-surgical therapy might result in more BOP reduction in the short term.
Mario Aimetti et al 2019 [54]	T:mechanical therapy in + with DL irradiation (setting 980 nm, 2.5 W, 10 kHz, pw, 30 s C: debridement using curettes and ultrasonic devices	Diode	Reported that adjunct use of DL did not yield any statistically significant clinical benefit as compared to nonsurgical mechanical treatment alone in controlling peri-implant inflammation at 3 months.

[MD:Mechanical Debridement, Er:YAG -erbium-doped yttrium aluminium garnet laser, DL- diode laser]

Photodynamic therapy

Photodynamic therapy includes the use of a low-power diode laser in combination with photosensitizing compounds. These components are linked to the bacterial membrane and, when excited, react with the substrate. The photosensitizer binds to the target cells and when it is irradiated with light of specific wavelength, in the presence of oxygen, it undergoes a transition from a low-energy ground state to an excited singlet state; then singlet oxygen and other very reactive agents are produced, which are toxic to these target cells .

The wave length range from 580 to 1400 nm and toluidine blue-(photosensitizer) concentrations between 10 and 50 ug/ml, photodynamic therapy generates bactericide effects against aerobic and anaerobic bacteria (such as Aggregatibacteractinomycetemcomitans, Porphyromonasgingivalis, Prevotella intermedia, Streptococcus mutans, Enterococcus faecalis) .

It has also been shown in vitro that photosensitization and light activation is more effective in killing bacteria from titanium surfaces than laser ablation alone.[55]

Table 7: Studies on photodynamic therapies in the treatment of peri implant diseases

Author And Year	Study Groups	Study Outcome
Esposito,2013[56]	Evaluate the adjunctive use of light-activated disinfection (LAD) in the treatment of peri-implantitis.	Adjunctive use of LAD therapy (FotoSan) with mechanical cleaning of implants affected by peri-implantitis did not improve any clinical outcomes when compared to mechanical cleaning alone up to 1 year after treatment.
Bassetti et al 2014 [44]	Compare the clinical, microbiological and host-derived effects in the non-surgical treatment of initial peri-implantitis with either adjunctive local drug delivery (LDD) or adjunctive photodynamic therapy (PDT) after 12 months.	Non-surgical mechanical debridement with adjunctive PDT was equally effective in the reduction of mucosal inflammation as with adjunctive delivery of minocycline microspheres up to 12 months. Adjunctive PDT may represent an alternative approach to LDD in the non-surgical treatment of initial peri-implantitis.
Rola Al Habashneh et al 2015[57]	PDT adjunct to mechanical therapy	Concluded that it is a new method for antibacterial treatment and may be used as an adjunct to or as conventional therapy for the treatment of periodontal and peri-implant diseases.
Mohammad Reza Karimit et al 2016[58]	Test (n):, MD + PDT Control (n): mechanical debridement using plastic curettes designed for implant surface.	The study of effectiveness of antimicrobial PDT on peri-implant diseases shows a statistically significant GI, BOP, PPD reductions as well as CAL gains.
Mongardini et al. 2017[59]	Test (n): 20 PDT + probiotics Control (n): 20 PDT + placebo	Both groups showed a comparable clinical peri-implant parameters at follow-up
M. Madi et al 2018 [60]	Test (n):, MD + PDT Control (n): , decontamination was performed afer full thickness fap refection by mechanical debridement using plastic	The results suggest that PDT and OFD have signifcantbenefts in peri-implantitis treatment by reducing bacterial count. Te presence of bacterial complex with diferent response to therapeutic

	curette OFD	modality suggests the use of combined decontamination methods for peri-implantitis treatment.
Alqahtani et al 2019 [61]	In smokers Test (n):, MD + PDT Control: MD	MD with adjunct aPDT is effective for the treatment of peri-implantitis. Routine oral hygiene maintenance plays a role in the overall success of MD with or without aPDT in patients with peri-implantitis.
H Wang, et al 2019 [62]	Test (n):, MD + PDT Control: no PDT	PDT combined with mechanical debridement significantly improves PD, PLI and SBI in participants with peri-implantitis. Importantly, PDT achieved a better CAL than mechanical debridement and cleaning.

[PDT –Photo Dynamic Therapy,MD-Mechanical Therapy,OFD-Open Flap Debridement,MD- Mechanical DEbridement]

Probiotics adjuvants to non-surgical therapy

Probiotics, as live microorganisms with antimicrobial and anti-inflammatory properties, have received increasing attention for their potential adjunctive effect in the treatment of peri-implant diseases.

Probiotics are beneficial to the host when administered in adequate amounts. They act through various mechanisms, including inhibition or competition with pathogens, production of antimicrobial substances, and adjustment of the mucosal immune system.

Recent research shows the use of different probiotics including Lactobacillus brevis (L. brevis) and Lactobacillus reuteri (L. reuteri) that have been assessed for their clinical efficacy in peri-implant disease .[63,64] According to the recent studies, these probiotics have a beneficial effect on the peri-implant inflammatory parameters.

Table 8: Studies on the effect of Probiotics in the treatment of peri implant diseases

Author/Study Design	Patient	Test Group: Type of probiotic administration; Frequency; Dosage	Control	Study outcomes
Flichy-Fernández A et al .2015 [63]	Peri – implant mucositis Nonsmoker	Lozenges Lactobacillus reuteri ATCC PTA 5289 + DSM 17938; x1; 1×108 CFU	Placebo	Significant improvement in clinical inflammatory parameters for probiotic group at follow-up
Hallstörm H et al., 2016[64]	Peri -implantitis Smokers	Lozenges- Lactobacillus reuteri DSM 17938 + ATCC PTA 5289; x2; 1×10^8 CFU	Placebo	No statistical significant differences between test and control groups at

				follow-up
Tada et al 2018[65]	Peri -implantitis Smokers;	Lozenges- Lactobacillus reuteri DSM 17938 + ATCC PTA 5289; x2; 1×10^8 CFU	Placebo	No statistical significant differences between test and control groups at follow-up
Galofré M et al 2018 [66]	Peri -implantitis	Lozenges- Lactobacillus reuteri DSM 17938 + ATCC PTA 5289; x1; 1×10^8 CFU	Placebo	No statistical significant differences between test and control groups of p-iM at follow-upNo statistical significant differences between test and control groups of PI at follow-up
Peña M et al 2019[67]	Peri – implant mucositis	Lozenges- Lactobacillus reuteri (DSM 17938 + ATCC PTA 5289; x1; NA	Placebo	No statistical significant differences between test and control groups at follow-up
Alqahtani et al. 2019 [68]	Peri – implant mucositis Non smoker	Lozenges- Lactobacillus reuteri (DSM 17938 + ATCC PTA 5289; x1; NA	Placebo	On a short-term basis, MD with adjunct PT is more effectual in the treatment of PiM than MD alone in never-smokers. Cigarette-smoking compromises peri-implant soft tissue healing following MD with or without adjunct PT.
Alqahtani et al. 2019 [49]	Peri – implant mucositis smoker	Lozenges- Lactobacillus reuteri (DSM 17938 + ATCC PTA 5289; x1; NA	Placebo	On a short-term basis, Cigarette-smoking compromises peri-implant soft tissue healing following MD with or without adjunct PT.

Laleman I et al 2020 [69]	Peri -implantitis	lozenges containing L. reuteri (ATCC PTA 5289 & DSM 17938),	Placebo	No adjunctive effects of the use of L. reuteri probiotics in the treatment of peri-implantitis were found.

Conclusion

Peri-implant diseases are indeed a challenge for the profession, from an etiologic, diagnostic, and therapeutic perspective. Among the treatment modalities non-surgical therapy is always the first-choice intervention in both peri implant mucositis and peri implantitis but may not be sufficient to treat advanced cases.Regardless of which therapeutic treatment protocol is adopted for the management of peri-implant diseases, Long-term maintenance is also an important criteria. Therefore, clinicians and patients must be prepared to accept a long-term, regular maintenance care to identify early signs of the disease and develop treatment strategies particularly for those at high risk.

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