



MTD

MedTechDental

MTD Scientific dossier

OVERALL BASE STUDIES FOR GELCIDE AND IMPLA LINES

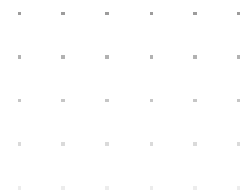
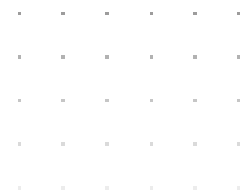


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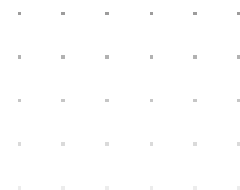
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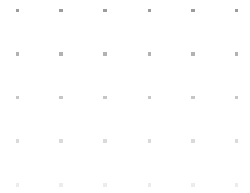
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Introduction

With this scientific dossier we would like to offer some very strong studies performed globally that support the scientific understanding of our claims of “protecting the dental bone”.

It's divided in 4 main parts, the first being the overall understanding of the current situation on periodontal diseases prevalence across the world, the importance of dentistry using (systemic) antibiotics that help existing treatments but fail to provide an income to the industry while, due to poor patient compliance, it generates a less predictable treatment outcome.

On the second part periodontitis is analyzed, with a strong focus on treatment options as well as outcomes.

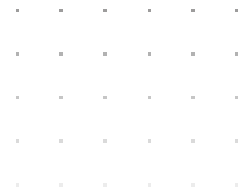
Part 3 is dedicated to peri-implantitis and peri-implant mucositis, citing several studies on these diseases.

Lastly, in part 4 several full studies are placed to go in depth on the key issues discussed.

This is a living document and we always appreciate contributions and support to it. Thanks in advance for taking the time to go through it.

Sincerely

The MTD team



Overall studies: Quantifying and identifying the prevalence of periodontal diseases and antibiotic usage in dentistry

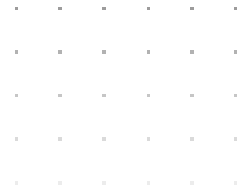
The clinical impact of bacterial biofilms.

Høiby N1, Ciofu O, Johansen HK, Song ZJ, Moser C, Jensen PØ, Molin S, Givskov M, Tolker-Nielsen T, Bjarnsholt T.

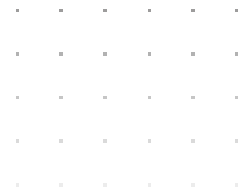
Int J Oral Sci. 2011 Apr;3(2):55-65. doi: 10.4248/IJOS11026.

Abstract

Bacteria survive in nature by forming biofilms on surfaces and probably most, if not all, bacteria (and fungi) are capable of forming biofilms. A biofilm is a structured consortium of bacteria embedded in a self-produced polymer matrix consisting of polysaccharide, protein and extracellular DNA. Bacterial biofilms are resistant to antibiotics, disinfectant chemicals and to phagocytosis and other components of the innate and adaptive inflammatory defense system of the body. It is known, for example, that persistence of staphylococcal infections related to foreign bodies is due to biofilm formation. Likewise, chronic *Pseudomonas aeruginosa* lung infections in cystic fibrosis patients are caused by biofilm growing mucoid strains. Gradients of nutrients and oxygen exist from the top to the bottom of biofilms and the bacterial cells located in nutrient poor areas have decreased metabolic activity and increased doubling times. These more or less dormant cells are therefore responsible for some of the tolerance to antibiotics. Biofilm growth is associated with an increased level of mutations. Bacteria in biofilms communicate by means of molecules, which activate certain genes responsible for production of virulence factors and, to some extent, biofilm structure. This phenomenon is called quorum sensing and depends upon the



concentration of the quorum sensing molecules in a certain niche, which depends on the number of the bacteria. Biofilms can be prevented by antibiotic prophylaxis or early aggressive antibiotic therapy and they can be treated by chronic suppressive antibiotic therapy. Promising strategies may include the use of compounds, which can dissolve the biofilm matrix and quorum sensing inhibitors, which increases biofilm susceptibility to antibiotics and phagocytosis.



Strategies for combating bacterial biofilm infections

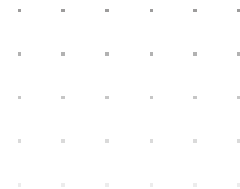
Hong Wu, Claus Moser, Hengzhuang Wang, Niels Høiby, Zhijun Song

International Journal of Oral Science (Impact Factor: 2.53). 12/2014; 7(1). DOI: 10.1038/ijos.2014.65

ABSTRACT

Formation of biofilm is a survival strategy for bacteria and fungi to adapt to their living environment, especially in the hostile environment. Under the protection of biofilm, microbial cells in biofilm become tolerant and resistant to antibiotics and the immune responses, which increases the difficulties for the clinical treatment of biofilm infections. Clinical and laboratory investigations demonstrated a perspicuous correlation between biofilm infection and medical foreign bodies or indwelling devices. Clinical observations and experimental studies indicated clearly that antibiotic treatment alone is in most cases insufficient to eradicate biofilm infections. Therefore, to effectively treat biofilm infections with currently available antibiotics and evaluate the outcomes become important and urgent for clinicians. The review summarizes the latest progress in treatment of clinical biofilm infections and scientific investigations, discusses the diagnosis and treatment of different biofilm infections and introduces the promising laboratory progress, which may contribute to prevention or cure of biofilm infections. We conclude that, an efficient treatment of biofilm infections needs a well-established multidisciplinary collaboration, which includes removal of the infected foreign bodies, selection of biofilm-active, sensitive and well-penetrating antibiotics, systemic or topical antibiotic administration in high dosage and combinations, and administration of anti-quorum sensing or biofilm dispersal agents. International Journal of Oral Science advance online publication, 12 December 2014; doi:10.1038/ijos.2014.65.

Strategies for combating bacterial biofilm infections (PDF Download Available). Available from: https://www.researchgate.net/publication/269774835_Strategies_for_combating_bacterial_biofilm_infections



Antibiotic prescribing practices by dentists: A review

Najla Saeed Dar-Odeh,¹ Osama Abdalla Abu-Hammad,¹ Mahmoud Khaled Al-Omiri,¹ Ameen Sameh Khraisat,¹ and Asem Ata Shehabi²

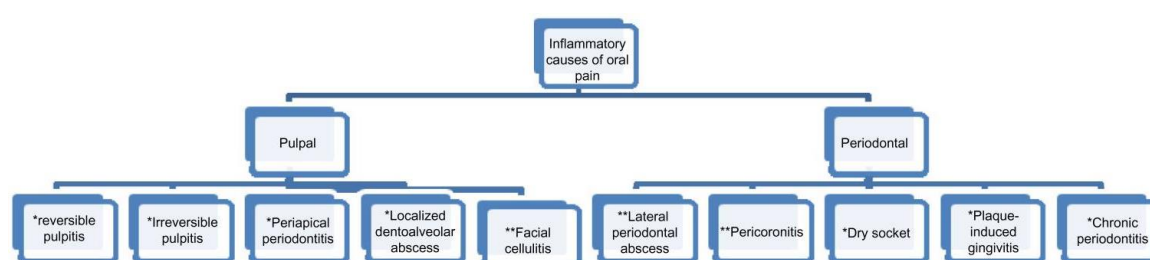
Theor Clin Risk Manag. 2010; 6: 301-306

Abstract

Antibiotics are prescribed by dentists for treatment as well as prevention of infection. Indications for the use of systemic antibiotics in dentistry are limited, since most dental and periodontal diseases are best managed by operative intervention and oral hygiene measures. However, the literature provides evidence of inadequate prescribing practices by dentists, due to a number of factors ranging from inadequate knowledge to social factors. Here we review studies that investigated the pattern of antibiotic use by dentists worldwide. The main defects in the knowledge of antibiotic prescribing are outlined. The main conclusion is that, unfortunately, the prescribing practices of dentists are inadequate and this is manifested by over-prescribing. Recommendations to improve antibiotic prescribing practices are presented in an attempt to curb the increasing incidence of antibiotic resistance and other side effects of antibiotic abuse.

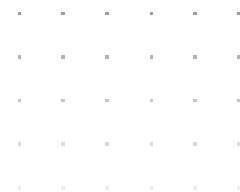
Recommendations

Recommended treatment modalities for common inflammatory oral conditions are shown in Figure 1.



Recommended treatment modalities for common inflammatory oral lesions.

Drainage is the recommended treatment for periapical periodontitis and for localized dentoalveolar abscess, with incisional drainage rather than via the root canal preferred.³¹



Empirical antibiotic therapy and drainage are recommended for more severe infections such as facial cellulitis, pericoronitis, lateral periodontal abscess, and necrotizing ulcerative gingivitis.

The type of antibiotic chosen and its dosing regimen are dependent upon the severity of infection and the predominant type of causative bacteria.

According to the BNF, amoxicillin is recommended for dental infections in doses ranging from 250 mg to 500 mg, every 8 hours.⁵⁰ The use of 3 g amoxicillin repeated after 8 hours is also mentioned, as a short course of oral therapy.⁵⁰ Another antibiotic that is also recommended by the BNF is co-amoxiclav, which can be used in doses ranging from 375 mg to 625 mg every 8 hours.⁵¹ In patients allergic to penicillin, clindamycin can be used in doses ranging from 150 mg to 450 mg every 6 hours.⁵² Another option for penicillin-allergic patients (as recommended by the BNF) is metronidazole, which can be used in a dose of 200 mg every 8 hours for 3–7 days.⁵³

For severe odontogenic infections, higher doses of a broad-spectrum antibiotic may be required. Lewis et al have shown that only 5% of the main isolates from dental abscesses are resistant to amoxicillin/clavulanic acid.⁵⁴ A more recent study found that bacteria associated with endodontic infections are completely susceptible to amoxicillin/clavulanic acid.⁵⁵ Furthermore, some researchers observed that amoxicillin/clavulanic acid and clindamycin are the only orally administered antimicrobials with adequate pharmacokinetic/pharmacodynamic properties to be effective against the most commonly isolated oral pathogens for the treatment of orofacial infections.³⁹ When amoxicillin/clavulanic acid is used, a dosing regimen of 1 g twice daily provides a successful clinical outcome, better patient convenience and compliance, and less gastrointestinal upset owing to the minimizing of the clavulanic acid dose.³⁹ As mentioned previously, patients can be seen after 2 or 3 days to determine whether treatment should be stopped or continued.

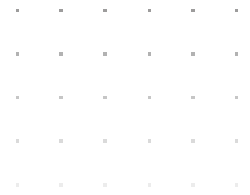
Patients who are allergic to penicillin should benefit from clindamycin; it is active against some oral anaerobes and facultative bacteria, and has the advantage of good bone penetration. However, increasing the dose may increase the possibility of serious side effects such as pseudomembranous colitis,^{56–58} Sweet's syndrome,⁵⁹ and neutropenia.⁶⁰

Infections in which anaerobic bacteria are implicated (such as pericoronitis, periodontal abscess and necrotizing ulcerative gingivitis) are better treated with metronidazole; the best dosage regimen in terms of pharmacodynamic/pharmacokinetic aspect is 250 mg every 8 hours.³⁹

Other inflammatory/painful oral conditions such as cracked tooth, dentine hypersensitivity, and bacterial sialadenitis are outside the scope of this review and their management is thoroughly explained in specialized references.

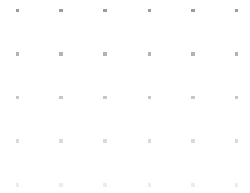
In addition to the proper dosing regimens and professionally responsible prescribing practices, the general public needs to be educated about the importance of restricting the use of antibiotics to only cases of severe infection. Patients have become accustomed to being given an antibiotic for a range of medical complaints. Unfortunately, patients presenting at dental surgeries also routinely expect an antibiotic for the treatment of 'toothache'.³

Dental patients not only pressure their dentist to get an antibiotic prescription, they also self-medicate. Self-medication with antibiotics was found to be alarmingly high in some developing countries.^{61–64} Also in Europe, self-prescription of antibiotics was reported, particularly in eastern and southern parts.^{65,66}



In conclusion, prescribing practices of dentists can be improved by increasing awareness among dental practitioners of the recommended guidelines. Furthermore, the importance of initiating awareness programs among the general public should not be overlooked.

[Link to full study](#)



Local and Systemic Levels of Tobramycin Delivered from Calcium Sulfate Bone Graft Substitute Pellets

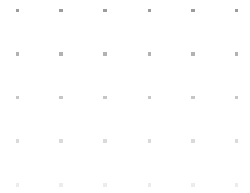
Thomas M. Turner, DVM; Robert M. Urban, AS; Deborah J. Hall, BS; Ping C. Chye, MD; John Segreti, MD; and Steven Gitelis, MD

[Clin Orthop Relat Res.](#) 2005 Aug;(437):97-104.

Abstract

We asked if tobramycin-loaded calcium sulfate pellets could be used to maintain high local site antibiotic concentrations for an extended period with minimal systemic levels and without adverse effects on vital organs. Calcium sulfate pellets loaded with 10% tobramycin were implanted in contained medullary defects in the proximal humeri of canines. The number of pellets implanted was calculated to yield an equivalent human maximum prescribed dose, and 1.8-fold this dose. These doses converted to approximately 20 mg/kg, and 36 mg/kg, respectively, for the canine. Local and systemic tobramycin levels, pellet resorption, bone response, clinical pathology parameters, and histopathologic responses of potential target organs were analyzed to determine if there was any adverse response for a 28-day period. Serum tobramycin was elevated for less than one day while local levels remained elevated for at least 14 days, and in some animals, 28 days. Tobramycin delivered locally from calcium sulfate pellets had no apparent adverse effect on clinical pathology parameters or on any of the organs that were analyzed. In addition, bone formation and pellet resorption followed patterns typically seen with calcium sulfate materials.

[Link to full study](#)



Prevalence of periodontitis in adults in the United States: 2009 and 2010.

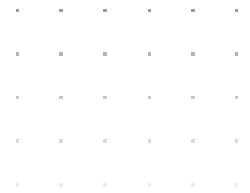
Eke PI, Dye BA, Wei L, Thornton-Evans GO, Genco RJ; CDC Periodontal Disease Surveillance workgroup: James Beck (University of North Carolina, Chapel Hill, USA), Gordon Douglass (Past President, American Academy of Periodontology), Roy Page (University of Washington)

J Dent Res. 2012 Oct;91(10):914-20. Epub 2012 Aug 30.

Abstract

This study estimated the prevalence, severity, and extent of periodontitis in the adult U.S. population, with data from the 2009 and 2010 National Health and Nutrition Examination Survey (NHANES) cycle. Estimates were derived from a sample of 3,742 adults aged 30 years and older, of the civilian non-institutionalized population, having 1 or more natural teeth. Attachment loss (AL) and probing depth (PD) were measured at 6 sites per tooth on all teeth (except the third molars). Over 47% of the sample, representing 64.7 million adults, had periodontitis, distributed as 8.7%, 30.0%, and 8.5% with mild, moderate, and severe periodontitis, respectively. For adults aged 65 years and older, 64% had either moderate or severe periodontitis. Eighty-six and 40.9% had 1 or more teeth with AL \geq 3 mm and PD \geq 4 mm, respectively. With respect to extent of disease, 56% and 18% of the adult population had 5% or more periodontal sites with \geq 3 mm AL and \geq 4 mm PD, respectively. Periodontitis was highest in men, Mexican Americans, adults with less than a high school education, adults below 100% Federal Poverty Levels (FPL), and current smokers. This survey has provided direct evidence for a high burden of periodontitis in the adult U.S. population.

Key link: http://www.healthindicators.gov/Indicators/Periodontal-disease-adults-45-74-years_1280/Profile/Chart_Bar_Demographics



Periodontal health in Europe: future trends based on treatment needs and the provision of periodontal services--position paper 1.

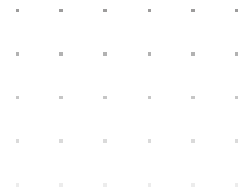
König J1, Holtfreter B, Kocher T.

Eur J Dent Educ. 2010 May;14 Suppl 1:4-24. doi: 10.1111/j.1600-0579.2010.00620.x.

Abstract

This review gives an update on recent epidemiologic data on periodontal diseases and a description of current periodontal services in Europe. A Medline search of articles published within the last decade with the keywords epidemiology, prevalence, periodontitis, tooth loss, and Europe was performed. Data on provision of dental services originated from international databases. Epidemiologic data on the prevalence of edentulism, the number of missing teeth, the prevalence of probing depth (Community Periodontal Index - CPI \geq 3 or Pocket Depth - PD \geq 4 mm), and clinical attachment loss (CAL \geq 4 mm) displayed a fragmentary picture within Europe. With respect to the limited data on periodontal health, Spain, Sweden, and Switzerland ranked as the healthiest among European countries in contrast to Germany where increased tooth loss and the highest prevalence of CAL \geq 4 mm were reported. The role of dental auxiliaries especially of dental hygienists and/or the medico-legal framework in which they work, appears to be an important factor in provision of effective periodontal care. Actual epidemiologic data on periodontal diseases are non-homogeneous and absent from several European countries. This emphasises the need for more national representative epidemiological studies with a uniform design to permit comparability between different nations. Merging actual epidemiologic data with former data on provision of periodontal care may help to explain differences in periodontal parameters on a population basis and to define future provision of dental care.

Some useful links to complement the information: <http://www.oralhealthplatform.eu/wp-content/uploads/2015/09/Report-the-State-of-Oral-Health-in-Europe.pdf> (page 21)



Prevalence of periodontitis in an adult population from an urban area in North Italy: findings from a cross-sectional population-based epidemiological survey.

Aimetti M1, Perotto S2, Castiglione A3, Mariani GM1, Ferrarotti F1, Romano F1.

J Clin Periodontol. 2015 Jul;42(7):622-31. doi: 10.1111/jcpe.12420. Epub 2015 Jun 25.

Abstract

AIM:

There is a paucity of up-to-date data regarding prevalence and risk indicators of periodontitis in Italy. Therefore, the aim of this study was to evaluate the prevalence of periodontitis and its risk indicators among adults from an urban area in North Italy.

MATERIAL AND METHODS:

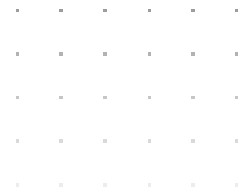
This cross-sectional survey used a stratified two-stage probability sampling method to draw a representative sample of the adult population of the city of Turin. About 1600 individuals, 20-75 years old, were randomly selected and 736 subjects agreed to participate (47% of the sampled subjects). Clinical parameters were assessed using a full-mouth protocol. Logistic models were applied to assess associations between periodontitis and its putative risk indicators. Age was included as restricted cubic spline.

RESULTS:

Based on CDC/AAP case definition, the prevalence estimates of severe and moderate periodontitis were 34.94% (95% CI: 31.23-38.74) and 40.78% (95% CI: 36.89-44.79). The probability of periodontitis increased in smokers (adjusted OR 2.06, 95% IC: 1.26-3.37, $p = 0.004$) and with age but leveled off in the 50+ year-old group ($p < 0.001$).

CONCLUSION:

Periodontitis was highly prevalent in the Turin population. The present data will enable development of appropriate public health programs and allocation of resources.



Supporting studies for Gelcide

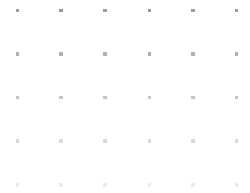
Primer for antimicrobial periodontal therapy.

[Slots J1.](#)

J Periodont Res 2002; 37; 389–398. Blackwell Munksgaard, 2002

Abstract

Successful prevention and treatment of periodontitis is contingent upon effective control of the periodontopathogenetic microbiota. Periodontal pathogens reside in subgingival sites but also colonize supragingival plaque, tongue dorsum and other oral sites. Controlling destructive periodontal disease warrants a comprehensive antimicrobial approach that targets periodontal pathogens in various ecological niches of the oral cavity. Also, to effectively combat periodontal pathogens, the various elements of antimicrobial periodontal therapy should be engaged within a short period of time. Scaling and root planing, with or without periodontal surgery, along with proper oral hygiene, constitute the primary approach to controlling periodontopathogens. Antimicrobial agents administered systemically or locally can help suppress periodontal pathogens in periodontal sites and in the entire mouth. Microbiological testing aids the clinician in selecting the most effective antimicrobial agent or combination of agents, and in monitoring the effectiveness of periodontal treatment. The present paper considers theoretical and practical aspects of effective antimicrobial treatment of destructive periodontal disease.



Identification of intracellular oral species within human crevicular epithelial cells from subjects with chronic periodontitis by fluorescence in situ hybridization.

Colombo AV1, da Silva CM, Haffajee A, Colombo AP.

J Periodontol Res. 2007 Jun;42(3):236-43.

Abstract

BACKGROUND AND OBJECTIVE:

Interactions between oral bacteria and gingival epithelial cells play an important role in the pathogenesis of periodontal diseases. This study used in situ hybridization with 16 rRNA probes and confocal microscopy to detect the periodontal pathogens *Porphyromonas gingivalis*, *Actinobacillus actinomycetemcomitans*, *Tannerella forsythia*, and *Treponema denticola* within epithelial cells from periodontal pockets, gingival crevice, and buccal mucosa collected from subjects with chronic periodontitis (n = 14) and good periodontal health (n = 8).

MATERIAL AND METHODS:

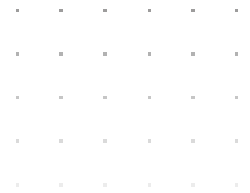
Each green fluorescent species-specific and universal probe was hybridized with all 58 epithelial samples from the 22 patients. The samples were observed by confocal microscopy to confirm the intracellular localization of oral species of bacteria. The mean frequency of detection and number of intracellular bacteria per epithelial cell were computed for each sample.

RESULTS:

The frequency of cells with internalized bacteria was higher in samples from the gingival crevice than in samples from the oral mucosa. Epithelial cells from all subjects harbored intracellular bacteria; however, patients with periodontitis presented significantly higher counts of bacteria per cell than periodontally healthy individuals ($p < 0.05$). Periodontal pathogens showed a trend to be detected in higher numbers in epithelial cells from periodontitis patients. In particular, *T. forsythia* and *T. denticola* were significantly more prevalent in periodontal pocket cells than healthy sulci and buccal cell samples in the periodontitis group ($p < 0.05$).

CONCLUSION:

Those findings indicate that crevicular and buccal cells present internalized bacteria, regardless of periodontal status. However, higher bacterial loads are detected in cells from subjects with periodontitis.



A systematic review on the effect of systemic antimicrobials as an adjunct to scaling and root planing in periodontitis patients.

Herrera D1, Sanz M, Jepsen S, Needleman I, Roldán S.

J Clin Periodontol. 2002;29 Suppl 3:136-59; discussion 160-2.

Abstract

BACKGROUND:

Scaling and root planing (SRP) are the bases of non-surgical therapy in the treatment of periodontitis. However, results from this therapy are often unpredictable and dependable from many different factors.

OBJECTIVES:

The aim of this systematic review was to evaluate the effectiveness of the adjunctive use of systemic antimicrobials with scaling and root planing (SRP) vs. SRP alone in the treatment of chronic (CP) or aggressive periodontitis (AgP).

SEARCH STRATEGY:

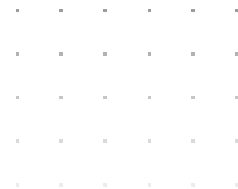
Use of computerized databases, namely MEDLINE, the Cochrane Oral Health Group Specialty Trials Register and EMBASE; reference lists from relevant articles were hand-searched; and a hand-search of selected journals until April 2001.

SELECTION CRITERIA:

Studies were selected if they were designed as controlled clinical trials in which systemically healthy patients with either AgP or CP were treated with SRP plus systemic antimicrobials in comparison with SRP alone or with placebo, for a minimum of 6 months. Main outcome measures were clinical attachment level (CAL) change and probing pocket depth (PPD) change.

DATA COLLECTION AND ANALYSIS:

Two reviewers extracted independently information regarding quality and study characteristics, in duplicate. Kappa scores determined their agreement. Main results were collected and grouped by drug, disease and PPD category. For the quantitative data synthesis, the data was pooled (when mean differences and standard errors were available), and either a Fixed Effects or Random Effects meta-analysis was used for the analysis.



RESULTS:

After an initial selection, 158 papers were identified by the manual and electronic searches; 25 papers were eligible for inclusion. Their quality assessment showed that randomization and allocation concealment methods were seldom reported and blindness was usually not defined clearly. In general, selected studies showed high variability and lack of relevant information for an adequate assessment. Overall, SRP plus systemic antimicrobial groups demonstrated better results in CAL and PPD change than SRP alone or with placebo groups. Only limited meta-analyses could be performed, due to the difficulties in pooling the studies and the lack of appropriate data. This analysis showed a statistically significant additional benefit for spiramycin (PPD change) and amoxicillin/metronidazole (CAL change) in deep pockets.

CONCLUSION:

Systemic antimicrobials in conjunction with SRP, can offer an additional benefit over SRP alone in the treatment of periodontitis, in terms of CAL and PPD change, and reduced risk of additional CAL loss. However, differences in study methodology and lack of data precluded an adequate and complete pooling of data for a more comprehensive analyses. It was difficult to establish definitive conclusions, although patients with deep pockets, progressive or 'active' disease, or specific microbiological profile, can benefit more from this adjunctive therapy.

Local Antibiotic Therapy in the Treatment of Bone and Soft Tissue Infections

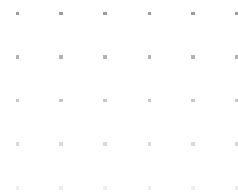
Stefanos Tsourvakas

"Selected Topics in Plastic Reconstructive Surgery", Edited by [Stefan Danilla](#), ISBN 978-953-307-836-6, 242 pages, Publisher: InTech, Chapters published January 20, 2012 under [CC BY 3.0 license](#)

Introduction

Bone and soft tissue infections are serious problems in orthopedic and reconstructive surgery. Especially, chronic osteomyelitis is a difficult infection to treat and eradicate. Long term parenteral antibiotics with multiple surgical debridements are often required for effective therapy (Cierny & Mader, 1984). Therefore, it is understandable that continuous efforts are being made and complete one or other element in the treatment of bone and soft tissue infections. There is a long history of local antibiotic use for the treatment of bone and soft tissue infections. During World

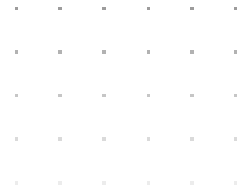
War I, Alexander Fleming observed that locally applied antiseptics failed to sterilize chronically infected wounds, but they did reduce the burden of bacteria (Fleming, 1920). In 1939, the instillation of sulfanilamide crystals, along with thorough debridement, hemostasis, primary closure and immobilization, resulted in a reduced infection rate for open fractures (Jensen et al, 1939). As additional systemic antimicrobial agents became available, interest in the topical treatment of wounds waned, but the management of established osteomyelitis remained problematic. In the 1960s, the method of closed wound irrigation-suction was popularized as a method which could be used to deliver high concentrations of an antibiotic after debridement (Dombrowski & Dunn, 1965). An alternative method for delivering high concentrations of an antibiotic to sites of lower extremity osteomyelitis was isolation and perfusion (Organ, 1971). The delivery of local antibiotics for the treatment of musculoskeletal infection has become increasingly popular for a variety of reasons. The basis for developing and using local antibiotic delivery systems in the treatment of bone and soft tissue infection is either to supplement or to replace the use of systemic antibiotics. High local levels of antibiotics facilitate delivery of antibiotics by diffusion to avascular areas of wounds that are inaccessible by systemic antibiotics and in many circumstances the organisms that are resistant to drug concentrations achieved by systemic antibiotic are susceptible to the extremely high local drug concentrations provided by local antibiotic delivery. The local use of antibiotics to prevent and treat bone and soft tissue infections was revived in Germany with the widespread use of prosthetic joint replacement, a situation in which infections were not anticipated consequence of trauma or sepsis but a devastating complication of elective surgery (Buchholz & Engelbrecht, 1970). However, it is from the www.intechopen.com 18 Selected Topics in Plastic Reconstructive Surgery year 2000 that research on local delivery of antibiotics to bone has gained considerable attention. Note that the numbers of publications in the last five years are double and decuple published in earlier decades (Soundrapandian et al, 2009). Bacterial infection in orthopedic and reconstructive surgery can be devastating, and is associated with significant morbidity and poor functional outcomes (Haddad et al, 2004). Operative treatments (excision of infected and devascularized tissues, obliteration of dead space, restoration of blood supply and soft tissue coverage, stabilization and reconstruction of the damaged bone), removal of all foreign bodies and systemic antimicrobial therapy are three crucial components of the treatment of these cases (Lazzarini et al, 2004). A long-term course of systemic antibiotherapy has been considered essential, but these prolonged therapies can result in side effects or toxicity. In order to achieve therapeutic drug concentration in the affected area, high systemic doses are generally required which can further worsen toxic side effects (Nandi et al, 2009). Antibiotic treatment may be inadequate or ineffective in patients with poorly vascularized infected tissues and osteonecrosis, which is often present in cases of osteomyelitis. Moreover, normal doses of systemic antibiotics may be insufficient to breach the glycocalyx or biofilm produced by the infecting bacteria (El-Husseiny et al, 2011). Despite intensive therapy, advances in surgical techniques, and development of new antimicrobials, relapse rate are still significant and treatment of bone and soft tissue infections remain challenging. New methods such as local delivery of antibiotics have evolved in an attempt to improve the prognosis of patients with musculoskeletal infections. The use of local antibiotic delivery system has become an accepted treatment method that continues to evolve for a variety of reasons. There has been an explosion of new technologies that are designed to facilitate the delivery of local antibiotics in new and creative ways. The primary reason for using these local antibiotic delivery vehicles is the ability to achieve very high local concentrations of antibiotics without associated systemic toxicity. In the



typical infected wound environment, which frequently has zones of avascularity, the ability to achieve high levels of antibiotics in these otherwise inaccessible areas is highly desirable (Cierny, 1999). Additional reasons for use of these delivery vehicles include the desire to treat remaining planktonic organisms and sessile organisms in biofilms more effectively with high concentrations of antibiotics (Hanssen et al, 2005). Because bone regeneration often is required as a part of the treatment plan, a recent trend has been simultaneously to provide a frame work of osteoinductive and osteoconductive materials along with antibiotics (Gitelis & Brebach, 2002). Despite the rapid acceptance of these antibiotic delivery vehicles, there are many unanswered questions related to their use, particularly when viewed within the environment of biofilms. Considerable investigation and development still are required to develop the necessary data to help determine a number of unknown variables associated with the use of local antibiotic delivery systems. In the application of a local antibiotic therapy for bone and soft tissue infections the following aspects should be considered: a) delivery technique; b) type of antibiotic that can be used; c) pharmacokinetics; d) possibility of application to a coating and to fillers; e) possibility of combination with osteoconductive and osteoinductive factors; f) use as prophylaxis and/or therapy; g) drawbacks. This review introduces bone and soft tissue infection-its present options for drug delivery systems and their limitations, and the wide range of carrier materials and effective drug choices. Also, I will describe and contrast the different local antibiotic delivery vehicles to www.intechopen.com Local Antibiotic Therapy in the Treatment of Bone and Soft Tissue Infections 19 provide a context for their current clinical use and to discuss the emerging investigate and developmental directions of these biomaterials

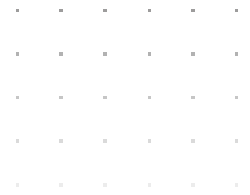
Conclusion

The appropriate use of antimicrobial agents has decreased morbidity and mortality from orthopedic-related infections. Although systemic antibiotic use has been used for many years, new methods of local antibiotic delivery may result in increased antibiotic levels, decreased toxicity, and possibly greater efficacy. Antibiotic impregnated polymethylmethacrylate beads www.intechopen.com 34 Selected Topics in Plastic Reconstructive Surgery are currently being used in a variety of applications, but this method requires a second procedure for removal of the antibiotic delivery system. There is considerable interest in finding methods of delivering effective doses of antimicrobial drugs locally, not only in orthopedics, but across a range of specialists. While most of the antibacterial agent contained within a biodegradable system may be eluted, only 25% is actually released from polymethylmethacrylate beads. Biodegradable materials could mimic bone substances like calcium phosphate based carriers can be chosen for local drug delivery system in osteomyelitis with potential clinical application in orthopedic surgery. Widespread research is currently being conducted in the area of local drug delivery systems to treat osteomyelitis. Despite this fact, much work is still desired in the areas of biodegradable and biocompatible materials, the kinetics of antibiotic release, and further development of current systems before many of these formulations can be used. The seer diversity of available systems and the lack of suitable trials comparing them in-vivo makes their evaluation difficult. Nonetheless, it is apparent that while collagen fleece is currently the most widely used antimicrobial carrier system, the duration of its antibiotic delivery is the shortest. Other delivery systems have shown greater promise, and these that are able both to stimulate the formation of new bone and provide a scaffold, such as composite antibiotic carriers, are most likely to gain widespread acceptance in the future. In future, researchers remain optimistic that many of these systems can be developed



with ideal zero-order release kinetics profiles, in-vivo, over long periods of time, allowing for widespread use in chronic osteomyelitis patients. By utilizing newer forms of sustained release antibiotic delivery systems, it will be possible to deliver such antibiotics at constant rates over a prolonged period of time and would eliminate the need for multiple dosing. It is hoped that in the future, development of new implantable systems would be helpful to reduce the cost of drug therapy, increase the efficacy of drugs, and could enhance the patient's compliance.

[Link to full study](#)



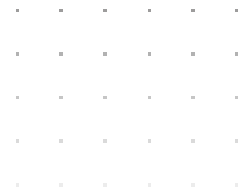
Topical and systemic antibiotics in the management of periodontal diseases.

Mombelli A, Samaranayake LP.

Int Dent J. 2004 Feb;54(1):3-14.

Abstract

Both systemic and topical antibiotics are increasingly used in the management of periodontal infections. Whilst these drugs are used mostly on an empirical basis, some contend that rational use of antibiotics should be the norm due to their wide abuse and consequential global emergence of antibiotic resistance organisms. Here we review the rationale and principles of antimicrobial therapy, treatment goals, drug delivery routes and various antibiotics that are used in the management of periodontal diseases. The pros and cons of systemic and local antibiotic therapy are described together with practical guidelines for their delivery. The available data indicate, in general, that mechanical periodontal treatment alone is adequate to ameliorate or resolve the clinical condition in most cases, but adjunctive antimicrobial agents, delivered either locally or systemically, can enhance the effect of therapy in specific situations. This is particularly true for aggressive (early onset) periodontitis, in patients with generalized systemic disease that may affect host resistance and in case of poor response to conventional mechanical therapy. Locally delivered antibiotics together with mechanical debridement are indicated for non-responding sites of focal infection or in localized recurrent disease. After resolution of the periodontal infection, the patient should be placed on an individually tailored maintenance care program. Optimal plaque control by the patient is of paramount importance for a favorable clinical and microbiological response to any form of periodontal therapy.



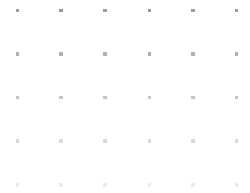
Metronidazole in periodontitis: reduced need for surgery.

Loesche WJ¹, Giordano JR, Hujoel P, Schwarcz J, Smith BA.

J Clin Periodontol. 1992 Feb;19(2):103-12.

Abstract

A considerable amount of circumstantial evidence indicates that most forms of periodontitis are due to the presence or dominance of a finite number of bacterial species in the subgingival plaque. Almost all of the putative pathogens are anaerobic species, indicating that most forms of periodontitis could be diagnosed as anaerobic infections. In this double-blind investigation, patients with elevated proportions or levels of spirochetes in 2 or more plaque samples, i.e., 60% spirochetes, were randomly assigned to receive either metronidazole, 250 mg 3 x a day for 1 week, or placebo (positive-control) after the completion of all debridement procedures. When the patients were re-examined 4 to 6 weeks later, the patients in the metronidazole group (n = 15) exhibited a highly significant (p less than 0.01) reduction in probing depth and apparent gain in attachment levels relative to the patients (n = 18) in the positive-control group about those teeth that initially had probing depths of 4 to 6 mm. This pattern was also observed about teeth that initially had probing depths greater than or equal to 7 mm. This reduction in probing depths and apparent gain in attachment was associated with a significant reduction in the need for periodontal surgery in the metronidazole-treated patients (difference 8.4 teeth per patient) compared to the positive-control patients (2.6 teeth per patient). These clinical improvements in the metronidazole group were associated with significantly lower proportions of spirochetes, selenomonads, motile rods, and *P. intermedius*, and a significantly higher proportion of cocci in the plaques. These findings indicate that systemic metronidazole, when given after all the root surface debridement is completed, leads to additional treatment benefits, including a reduced need for surgery, beyond that which can be achieved by debridement alone.



A comparative evaluation of the clinical effects of systemic and local doxycycline in the treatment of chronic periodontitis

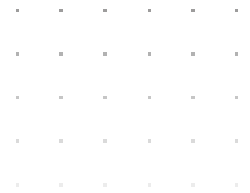
*Ferda Alev Akalın§, Esra Baltacıoğlu§, Dilek Sengün§, Süeda Hekimoğlu†, Müge Taskın†, Iker Etikan‡ and Inci Fisenk**

J Oral Sci. 2004 Mar;46(1):25-35

Abstract:

In this study, the clinical efficacies of systemic doxycycline (SD) and local doxycycline (LD) in the treatment of chronic periodontitis were compared. Forty-five patients were studied in 3 main groups with 5 treatments: SD alone, SD + scaling-root planing (SD+SRP), LD alone, LD+SRP and SRP alone. Antibiotic-treated patients were given doxycycline treatment alone in 1 quadrant of their upper jaws, and doxycycline + SRP was given in the contralateral quadrant. The areas included at least 4 teeth with ≥ 5 mm pockets. Probing depth (PD), clinical attachment level, gingival index, sulcular bleeding index and plaque index values were recorded at baseline and the 7th week. The results were statistically analyzed. All of the clinical parameters were significantly reduced by all treatments ($P \leq 0.05$). The SD and LD treatments alone provided significant clinical healings. The significant differences among the groups were only in PD at the 7th week. The LD treatment provided significantly higher PD reduction than the SD treatment ($P \leq 0.05$). No significant difference was found between the SD+SRP and the LD+SRP treatments. There was no significant difference between SD+SRP and SRP alone treatment ($P > 0.05$). The SD group showed lower PD reduction than SRP group ($P \leq 0.05$), while no significant difference was found between LD and SRP treatments. The LD alone treatment seemed more effective than SD alone treatment on PD reduction, but no significant difference was found between them when combined with the SRP. LD may be more preferable than SD as an adjunct to mechanical treatment since LD seems more effective than SD on PD reduction and does not have the side effects of SD. (J. Oral Sci. 46, 25-35, 2004)

[Link to the full study](#)



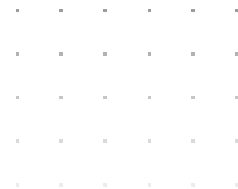
Antimicrobial advances in treating periodontal diseases.

Mombelli A1.

Front Oral Biol. 2012;15:133-48. doi: 10.1159/000329676. Epub 2011 Nov 11

Abstract

Antibiotics are generally an efficient means of treating bacterial infections, and therefore are an obvious candidate in the treatment of periodontal diseases. Systemically and locally administered antimicrobial agents of all kinds have been evaluated in multiple clinical trials. The vast majority of studies have tested antibiotics as adjuncts to non-surgical debridement. No regime has demonstrated superiority over systemically administered amoxicillin and metronidazole in the treatment of any clinically or microbiologically defined variant of periodontal disease. The frequency and consequences of adverse effects of antibiotics have always to be balanced against the potential consequences of not rapidly suppressing a periodontal infection. Proposed strategies to reduce the risk of bacterial antimicrobial resistance include: prescribing two drugs with a synergistic or complementary effect, the administration of antibiotics at a high dose for a short period, a combined approach with mechanical debridement to disrupt biofilms, and the focus on therapeutic rather than prophylactic use. Derivatives of existing antibiotic classes and new compounds that act on unique targets are the subject of preclinical investigations with a focus on action against antibiotic-resistant medical pathogens. In light of the excellent results of a combination therapy with well-established drugs that are cheap and efficient, clinical trials should compare newly proposed protocols for periodontal therapy to a positive control. Future studies should focus not only on the action against the microorganisms directly involved in periodontal diseases, but also on those relevant to other medical concerns.



Magic Bullet to treat Periodontitis: A targeted approach

Vidya Dodwad, Shubra Vaish, Mehak Chhokra, Aakriti Mahajan

JOURNAL OF PHARMACEUTICAL AND BIOMEDICAL SCIENCES, JPBMS, 2012, 20 (19)

Abstract:

Periodontitis is a disease attributable to multiple infectious agents and interconnected with cellular and humoral host responses. It results from extension of the inflammatory process initiated in the gingiva to the supporting periodontal tissues. Periodontal pockets provide natural reservoir bathed by gingival crevicular fluid that is easily accessible for the insertion of a delivery device. Controlled release delivery of antimicrobials is a therapeutic intervention directly into periodontal pockets and is available in various forms like gels, monolithic devices, irrigation systems, chips, films, strips,

microspheres, fibres etc. It is an effective monotherapy that has evoked a great interest and appears to hold a sound promising result in periodontal treatment. It does not substitute the local instrumentation but acts as an adjunct to it.

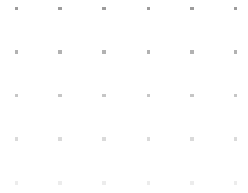
These local agents bypass the adverse effects of systemically administered antimicrobial agents, as well stabilize the attachment apparatus and reduce the probing depth thereby allowing better control and management of periodontal disease.

Conclusion

There are several drugs such as metronidazole, tetracycline, doxycycline, azithromycin, minocycline, chlorhexidine as well as herbal products like neem, pomegranate, propolis that are used and are also under further trial for their administration as local drug into the periodontal pocket.

Prudent administration of antimicrobial agents following judicious pharmacologic principles will preclude the abuse of chemotherapeutic agents and reduce the potential of developing or selecting drug resistant bacterial strains.

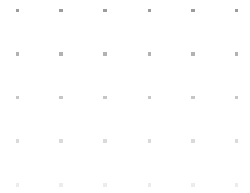
Local drug delivery system with controlled release properties have the potential to be used as a therapeutic component in the management of periodontal diseases. It aims to minimize drug degradation and loss, prevent harmful side-effects and increase drug bioavailability and



the fraction of the drug accumulated in the required zone.

Various drug delivery and drug targeting systems are currently under development to obtain increased dissolution velocity, increased saturation solubility, improved bioadhesivity and versatility in surface modification so that better and effective administration of desired and newer drug can be done through the best possible system.

[Link to the full study](#)



Effect of local drug delivery in chronic periodontitis patients: A meta-analysis

Rupali Kalsi, K. L. Vandana, Shobha Prakash

J Indian Soc Periodontol. 2011 Oct-Dec; 15(4): 304–309.

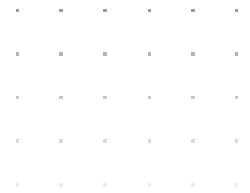
Abstract:

Periodontal diseases are multi-factorial in etiology, and bacteria are one among these etiologic agents. Thus, an essential component of therapy is to eliminate or control these pathogens. This has been traditionally accomplished through mechanical means (scaling and root planing (SRP)), which is time-consuming, difficult, and, sometimes, ineffective. From about the past 30 years, locally delivered, anti-infective pharmacological agents, most recently employing sustained-release vehicles, have been introduced to achieve this goal. This systematic review is an effort to determine the efficacy of the currently available anti-infective agents, with and without concurrent SRP,

in controlling chronic periodontitis. Four studies were included, which were all randomized controlled trials, incorporating a total patient population of 80, with 97 control sites and 111 test sites. A meta-analysis completed on these four studies including SRP and local sustained-release agents compared with SRP alone indicated significant adjunctive probing depth (PD) reduction for 10% Doxycycline hyclate (ATRIDOX), minocycline hydrochloride (ARESTIN), tetracycline hydrochloride (PERIODONTAL PLUS AB), and chlorhexidine gluconate (PERIOCHIP). Essentially, all studies reported substantial reductions in gingival inflammation, plaque scores, and bleeding indices, which were similar in both the control and the experimental groups. Use of antimicrobial sustained-release systems as an adjunct to SRP does not result in significant patient-centered adverse events.

Local drug delivery combined with SRP appears to provide additional benefits in PD reduction compared with SRP alone.

[*Link to the full study*](#)



Clinical and microbiological results following nonsurgical periodontal therapy with or without local administration of piperacillin/tazobactam

Marc Lauenstein & Marion Kaufmann & G. Rutger Persson

Clin Oral Investig. 2013 Sep;17(7):1645-60. doi: 10.1007/s00784-012-0856-4. Epub 2013 Jan 20

Abstract

Objectives

We assessed if adjunct administration of piperacillin/tazobactam added clinical and microbiological treatment benefits.

Materials and methods

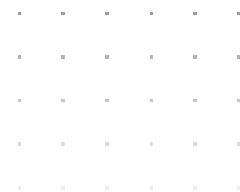
Thirty-six subjects (mean age 52.1years (SD±10.3)) (NS by group) with chronic periodontitis were randomly enrolled receiving subgingival debridement and the local administration of piperacillin/tazobactam (test group) or debridement alone (control group). Bleeding on probing (BOP), probing pocket depth (PPD), and microbiological counts of 74 species were studied by checkerboard DNA-DNA hybridization up to month 6 after treatment.

Results

Mean PPD changes between baseline and month 6 in the test and control groups were 1.5 and 1.8 mm, respectively (NS between groups). BOP in both groups decreased from about 80 to 40 %. At 4 and 12 weeks, lower counts of the following bacteria were found in the test group (site level): *Fusobacterium* species, *Parvimonas micra*, *Pseudomonas aeruginosa*, *Staphylococcus aureus*, *Tannerella forsythia*, *Treponema denticola*, and a composite load of nine pathogens ($p < 0.001$). At week 26, subjects receiving local antibiotics had a lower prevalence at tested sites for *Fusobacterium nucleatum* sp. polymorphum, *Fusobacterium periodonticum*, *P. micra*, and *T. denticola*.

Conclusions

At 26 weeks, treatment with or without piperacillin/tazobactam resulted in similar BOP and PPD improvements. At week 26 and at the subject level, the prevalence of 4/74 pathogens was found at lower counts in the group receiving local antibiotics.



Clinical relevance

Administration of piperacillin/tazobactam reduces the prevalence of *Fusobacterium*, *P. micra*, and *T. denticola* to a greater extent than debridement alone but with no short-term differences in PPD or BOP.

Discussion

There are currently no other clinical data on the efficacy to reduce bacterial counts in periodontal pockets by a single administration of piperacillin/tazobactam in subjects with moderate to advanced periodontitis. *P. gingivalis* was chosen as the target pathogen and as the primary outcome measure because it has been studied extensively in association with periodontitis [8, 23–25, 30, 35, 37]. Several other bacterial species demonstrated a greater susceptibility to the intervention in the test group and this effect remained also at week 26 for some species but not for *P. gingivalis*, *T. forsythia*, or *A. actinomycetemcomitans*.

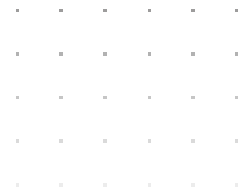
The limitation of the present study is that the control subjects were not treated with a placebo drug administration. Nevertheless, the clinical examiner and the laboratory staff members were blinded to the protocol assignment to control for bias. Another limitation is that the evidence of bacterial changes

following periodontal interventions from other studies does not easily provide information that can be utilized for statistical power analysis. Thus, we assumed based on our laboratory experiences that a 20–25 % difference could be anticipated. A decrease amounting to approximately 20–25% was obtained in the test group at weeks 2 and 4 for *P. gingivalis* and *P. aeruginosa*. At week 26, this remained the case for *P. aeruginosa*, suggesting that the administration of piperacillin/tazobactam has a relevant effect but limited to the control of *P. aeruginosa* subgingival colonization. One of the reasons why the reduction in bacterial counts was limited may be the result of less than optimal control of gingival inflammation as noticed by the rather high proportion of BOP at study endpoint.

The decreases in PPD and BOP obtained in the present study are consistent with the other studies on subgingival debridement not using antibiotics [1–7]. The extent of PPD reduction and decrease in BOP in the present study suggested a clinical effective outcome of therapy provided in both groups.

Furthermore, the extent of PPD reduction in both study groups in the present study was comparable, or greater to PPD reductions after combined local debridement and local antibiotics in other studies [30, 50]. In the present study, we treated subjects who were diagnosed with moderate to severe chronic periodontitis, and we only assessed interproximal conditions. In other similar studies, periodontal sites with more shallow PPDs have been studied [18, 21, 38]. It is well known that the

reduction of PPD in the range of 1.5 to 2.0mm can be obtained by debridement alone in deep periodontal pockets [1–3]. The extent of possible probing depth reduction may also be limited by



anatomical factors such as the extent and topography of alveolar bone loss and attachment loss. Some data have shown that local administration of doxycycline or minocycline in addition to debridement in subjects who smoke results in greater reduction in the frequency of *P. gingivalis* [22, 25]. In the present study, smoking did not seem to have an impact on the study outcomes neither on PPD nor BOP changes or microbiological changes. This may be explained by the low prevalence of smokers in the study.

Smoking, subject age, and gender were included as covariates in the subject-based analysis but did not significantly influence the results.

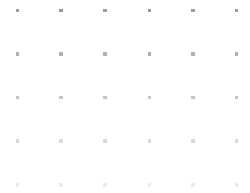
Although subject-based factors must be considered, it is generally perceived that chronic periodontitis is tooth/site specific [13–17]. In the present study, each subject contributed four individual test sites representing the sites with the most advanced periodontitis. Thus, no subject was overrepresented

providing more data than any other subject. Several studies have used site-based analysis and performed microbiological sampling only from mesio-buccal surfaces [8, 22, 24, 50–56]. There appears to be a defined order in bacterial species succession in early supragingival and subgingival biofilm redevelopment after professional cleaning. The site-specific development of periodontitis may be the result of the symbiotic effects due to co-aggregation in subgingival biofilms including *P. gingivalis*, *T. denticola*, and *T. forsythia* [53]. Thus, the presence and counts of *P. gingivalis*, *T. denticola*, and *T. forsythia* may suggest the stability of periodontal conditions at individual sites at teeth. The observations that local treatment with antibiotics can reduce the counts of these species are important [31, 50]. In the present study, the adjunct administration of piperacillin/tazobactam resulted in more reduction of not only *P. gingivalis*, *T. denticola*, and *T. forsythia* but also other species associated with co-aggregation in biofilms (i.e., *F. nucleatum*) and other bacteria that are associated with several diseases (*P. aeruginosa* and *S. aureus*) and identified not only in periodontitis but also in subjects with

peri-implantitis [48, 57–60].

It should also be noticed that the changes in bacterial counts over time were not consistently the same by different species. This may reflect the fluctuating state of bacterial growth and changes in the development of biofilms at different sites from which samples were taken. To some extent, it may also reflect measurement errors in sampling which might be the greatest error and by the laboratory procedures. The fact that the bacterial counts of *P. aeruginosa* and *S. aureus* at study endpoint did not differ by study group could be viewed as a positive finding in that these two species did not show evidence in counts that might suggest antibiotic resistance or other advantages by the medication.

The present study identified that without the use of the antibiotic, limited changes were found after debridement among the target bacteria. Recolonization of bacteria also occurred in the test group, and this is consistent with other studies [35]. Recolonization of bacteria following periodontal surgery in newly established shallow periodontal pockets also occurs soon after surgery [60]. This is consistent with the general concept that mechanical elimination of bacteria in a biofilm is not possible. Oral bacteria in biofilm comprise a complex community depending on the interface between the host and the microbial community as a whole [61]. Elimination of bacteria associated with periodontitis may therefore not be possible using local administration of antibiotics [32]. In addition to plasmid transfer and antibiotic resistance, there is a mechanical



protective glycolax layer that protects the biofilm and prevents penetration of antibiotics, and debridement may not effectively eliminate this glycolax in deep periodontal pockets.

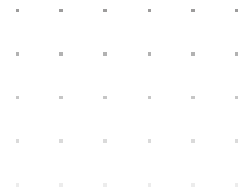
In the present study, high counts of *P. aeruginosa* were found in the post-treatment findings in subjects in the control group. While piperacillin/tazobactam appears to be effective against *P. aeruginosa* [43, 44], this may explain why lower counts of *P. aeruginosa* were found in the test groups.

In the present study, high counts of *A. actinomycetemcomitans* were found both at baseline and especially throughout the study in the control group, suggesting that subgingival debridement alone cannot significantly reduce or eliminate this microorganism. This observation is consistent with other studies suggesting that *A. actinomycetemcomitans* is difficult to manage through mechanical debridement alone [32, 62, 63]. The reduction of *A. actinomycetemcomitans* was, however, also limited in the test group. Although bacteria commonly viewed as putative pathogens in periodontitis, i.e., *T. forsythia* and *P. gingivalis*, were similarly affected by study procedures, the pathogenic capacities of *P. micra*, *Fusobacterium* species, and *T. denticola* should not be minimized. The lower prevalence of these species in the test group should be considered as having a beneficial impact on periodontal status. There are many studies to suggest that *P. micra*, *Fusobacterium* species, and *T. denticola* are present at high counts in cases with periodontitis (i.e., [8–10]).

In conclusion, the present study identified similar improvements in clinical periodontal outcomes at week 26 in subjects treated with nonsurgical debridement with or without a onetime administration of a local antibiotic (piperacillin/tazobactam).

At the subject level, the local antibiotic therapy controlled the colonization of *T. denticola*, *F. nucleatum polymorphum*, *F. periodonticum*, and *P. micra*.

[*Link to the full study*](#)



Supporting studies for the Impla line

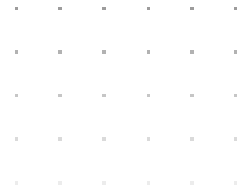
Management of peri-implantitis

Jayachandran Prathapachandran¹ and Neethu Suresh¹

Dent Res J (Isfahan). 2012 Sep-Oct; 9(5): 516–521

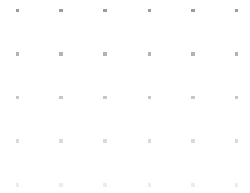
Abstract

Peri-implantitis is a site-specific infectious disease that causes an inflammatory process in soft tissues, and bone loss around an osseointegrated implant in function. The etiology of the implant infection is conditioned by the status of the tissue surrounding the implant, implant design, degree of roughness, external morphology, and excessive mechanical load. The microorganisms most commonly associated with implant failure are spirochetes and mobile forms of Gram-negative anaerobes, unless the origin is the result of simple mechanical overload. Diagnosis is based on changes of color in the gingiva, bleeding and probing depth of peri-implant pockets, suppuration, X-ray, and gradual loss of bone height around the tooth. Treatment will differ depending upon whether it is a case of peri-implant mucositis or peri-implantitis. The management of implant infection should be focused on the control of infection, the detoxification of the implant surface, and regeneration of the alveolar bone. This review article deals with the various treatment options in the management of peri-implantitis. The article also gives a brief description of the etiopathogenesis, clinical features, and diagnosis of peri-implantitis. Peri-implantitis is a site-specific infectious disease that causes an inflammatory process in soft tissues, and bone loss around an osseointegrated implant in function. The etiology of the implant infection is conditioned by the status of the tissue surrounding the implant, implant design, degree of roughness, external morphology, and excessive mechanical load. The microorganisms most commonly associated with implant failure are spirochetes and mobile forms of Gram-negative anaerobes, unless the origin is the result of simple mechanical overload. Diagnosis is based on changes of color in the gingiva, bleeding and probing depth of peri-implant pockets, suppuration, X-ray, and gradual loss of bone height around the tooth. Treatment will differ depending upon whether it is a case of peri-implant mucositis or peri-implantitis. The management of implant infection should be focused on the control of infection, the detoxification of the implant surface, and regeneration of the alveolar bone. This review article deals with the various treatment options in the management of peri-



implantitis. The article also gives a brief description of the etiopathogenesis, clinical features, and diagnosis of peri-implantitis.

Link to the full article: <http://www.ncbi.nlm.nih.gov/pmc/articles/PMC3612185/>



The epidemiology of peri-implantitis.

Mombelli A1, Müller N, Cionca N.

Clin Oral Implants Res. 2012 Oct;23 Suppl 6:67-76. doi: 10.1111/j.1600-0501.2012.02541.x.

Abstract

AIM:

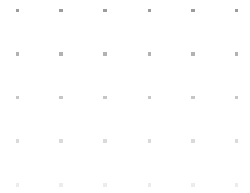
1. To review the literature on the prevalence and incidence of peri-implantitis.

METHODS:

Out of 322 potentially relevant publications we identified 29 articles concerning 23 studies, with information on the presence of signs of peri-implantitis in populations of at least 20 cases.

RESULTS AND CONCLUSIONS:

All studies provided data from convenience samples, typically from patients who were treated in a clinical center during a certain period, and most data were cross-sectional or collected retrospectively. Based on the reviewed papers one may state that the prevalence of peri-implantitis seems to be in the order of 10% implants and 20% patients during 5-10 years after implant placement but the individual reported figures are rather variable, not easily comparable and not suitable for meta-analysis. Factors that should be considered to affect prevalence figures are the disease definition, the differential diagnosis, the chosen thresholds for probing depths and bone loss, differences in treatment methods and aftercare of patients, and dissimilarities in the composition of study populations. Smoking and a history of periodontitis have been associated with a higher prevalence of peri-implantitis.



Effectiveness of implant therapy in Sweden

Jan Derks

J Dent Res. 2015 Mar;94(3 Suppl):44S-51S. doi: 10.1177/0022034514563077

Abstract

Dental implants are commonly used in restorative therapy in patients with partial or full edentulism. Knowledge regarding the outcome of this kind of treatment has been limited to evaluations of efficacy, i.e. therapy performed under optimal conditions. The current series of studies evaluated effectiveness of dental implant therapy including patient-reported outcomes, the occurrence of implant loss as well as peri-implantitis.

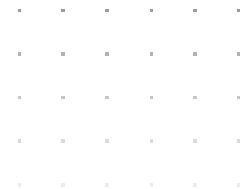
Using the national data registry of the Swedish Social Insurance Agency, 4,716 patients were randomly selected. All had been provided with implant-supported restorations in 2003/2004. Patient-reported outcomes were analyzed by questionnaire 6 years after completion of therapy (Study I). Patient files of 2,765

patients were collected from more than 800 clinicians. Information on patients, treatment procedures, and outcomes related to the implant-supported restorative therapy was extracted from the files. 596 of the 2,765 subjects attended a clinical examination 9 years after therapy. Early implant loss was assessed in patient files,

while late implant loss was recorded at the clinical examination (Study II). The prevalence of peri-implantitis was determined from clinical and radiographic data collected at the 9-year examination (Study III). Radiographs obtained from the patient files were used to evaluate the onset and pattern of progression of peri-implantitis (Study IV).

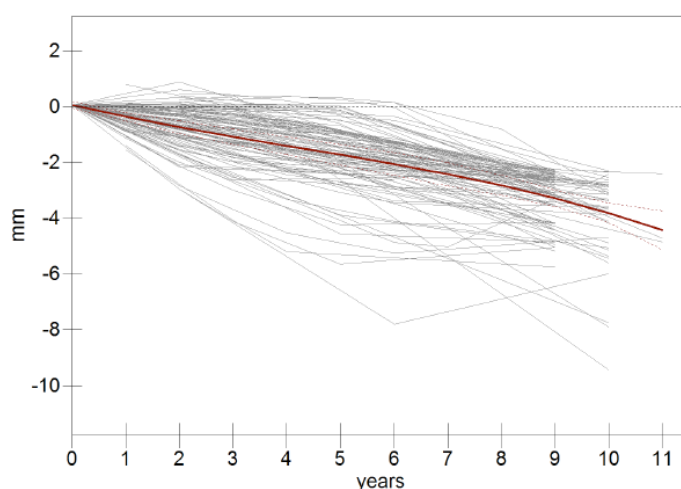
It was demonstrated that:

- the overall patient satisfaction was high but influenced by (i) age and gender of the patient, (ii) the extent of restorative therapy and (iii) the training of the clinician performing the treatment (Study I).
- implant loss occurred in 7.6% of all patients over a follow-up of 9 years; patient and implant characteristics influenced the outcome (Study II).
- 14.5% of all patients exhibited moderate/severe peri-implantitis, and several patient- and implant-related characteristics were identified as risk indicators (Study III).
- progression of peri-implantitis occurred in a non-linear, accelerating pattern, and, in the majority of cases, the onset of the disease had occurred early (Study IV).



Pattern progression of peri-implantitis as a degenerative condition

Figure 16. Estimated pattern of bone loss for each implant diagnosed with moderate/severe peri-implantitis at the 9-year examination (n=105, implants with ≥ 3 radiographic measurements); the red regression line indicates the mean estimated bone loss over time including the 95% CI



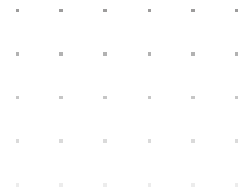
Findings

Patient-reported outcome measures

Results from the assessments of PROMs (Study I) indicated a high degree of patient satisfaction with implant-supported restorations. These findings are in agreement with reports from studies covering similar periods of follow-up (Pjetursson et al., 2005; Simonis et al., 2010). Thus, it may be concluded that the large majority of patients are satisfied with long-term outcomes of implant therapy. It is noteworthy that the perception of patients treated under everyday conditions was similar to perceptions described in studies on cohorts treated in specialist clinics.

Implant loss

The proportion of patients experiencing implant loss reported in Study II is in general agreement with the few studies presenting patient level data following different follow-up periods. Roos-Jansåker et al. (2006a), after 9 to 14 years, and Jemt et al. (2014), after 1 to 28 years, both recorded implant loss in 10.1% of patients. Balshe et al. (2009) found that 8.6% of patients had lost at least one implant after 2 to 7 years of follow-up. It is noteworthy that the proportion of implant loss in the present patient cohort (7.6%) compares favorably to results reported in above-mentioned



studies, all describing patient samples treated in specialist clinics. On the other hand, the one registry study published (Antalainen et al., 2013) reported lower numbers of implant loss (3.1% of patients affected) than the present cohort study. This discrepancy between the study from Finland and the present findings may be related to the validity of the data in the Finnish registry. It also supports the concept that registry studies should be complemented by clinical examinations for validation.

The level of training of the surgeon has been discussed as an important factor for failure rates in implant dentistry. Albrektsson et al. (2012) stated that, when experienced, well-trained clinicians are involved in the therapy, the collective rate for implant loss and peri-implantitis over 10 years is expected to be below 5% on

the implant level. In the present patient cohort, the level of clinical training (specialist vs. general practitioner) did not influence the odds for implant loss or peri-implantitis. In fact, 22% of all patients in the present sample received (surgery) their implants in a general practice setting, and implant loss in this subgroup was not different from outcomes in patients treated in specialist clinics.

In the analysis of risk indicators of implant loss, we included a multitude of potential factors. While we controlled for the extent of therapy, augmentation, number of implants, etc., we were not able to adjust for the inherent complexity of each individual case. It may be assumed that more complicated clinical situations

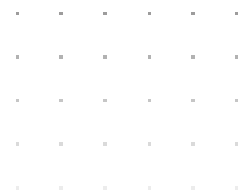
were handled by more experienced clinicians. Therefore, the observed lack of differences between categories of clinicians may have been confounded by the complexity of cases not considered in the statistical analysis.

Peri-implantitis

While almost 50% of all patients presented with clinical and radiographic signs of peri-implantitis at the 9-year examination, a subgroup of 14.5% was diagnosed with moderate/severe peri-implantitis (Study III). Moderate/severe peri-implantitis entailed, in addition to soft tissue inflammation, a crestal bone loss

exceeding 2 mm. These affected implants (8% of all implants) had, on the average, lost 29% of their bone support. The overall estimate of peri-implantitis, including inflammation and crestal bone loss >0.5 mm, on the patient level (45%) was considerably higher than results obtained from a recent meta-analysis

presented by Derks & Tomasi (2015). The authors reported a weighted mean patient prevalence of 22% (95% CI: 14–30%). This lower proportion of peri-implantitis is in agreement with our findings on the prevalence of moderate/severe peri-implantitis. Furthermore, it was stated in the review that the case definitions for peri-implantitis applied in the different studies influenced the reported disease prevalence. We used the radiographic thresholds suggested by Koldslund et al. (2010; 2011) and found similar proportions of overall and moderate/severe peri-implantitis. Eke et al. (2012; 2015) reported that 8% of all adults above the age of 30 exhibited signs of advanced periodontitis (≥ 2 interproximal sites with ≥ 6 mm attachment loss and ≥ 1 interproximal sites with ≥ 5 mm PPD). The corresponding value for moderate/severe peri-implantitis in the present project was 14.5%. In this context it should be realized that, even though the prevalence of the two



diseases - periodontitis and peri-implantitis - appears similar, important histopathological differences between the two disorders exist (Berglundh et al., 2011; Carcuac and Berglundh, 2014).

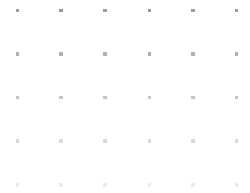
The results of Study IV were generated from a statistical model and indicated that the majority of patients diagnosed with moderate/severe peri-implantitis at the 9-year examination showed early signs of crestal bone loss already after 3 years.

This may indicate that bone loss, as part of peri-implantitis, may start early following implant placement and, if not treated, may progress over time. This is in general agreement with findings presented by Fransson et al. (2010) and Cecchinato et al. (2014) but stands in apparent contrast to results by Koldslund et al. (2010), who identified groups exhibiting different levels of disease severity but no differences in mean follow-up time.

Consequences of complications

It is obvious that the consequences of a complication, rather than the diagnosis itself, may be the primary concern of the patient. Results from Study II demonstrated that early and late implant loss entailed potentially severe consequences for the majority of patients, ranging from changes in treatment planning to complete loss of applied restorations. Health economics of implant loss and peri-implantitis were not analyzed in the current studies, but it may be assumed that costs associated with complications were high, both for the patient, for the clinician and providers of health insurance. Zitzmann et al. (2013) compared the cost-effectiveness of tooth-supported 3-unit restorations and single implants in the anterior dentition. The implant-supported solutions were found to be more cost-effective in a probability model based on an average observation period of 4 years. Results from Studies III & IV indicated that peri-implantitis is common and that its onset and progression may be time-dependent. Therefore, the 4-year observation period in the study by Zitzmann et al. (2013) may have underestimated the effects of peri-implantitis, particularly the costs related to its treatment. In two separate 10-year reports, Rocuzzo et al. (2012; 2014) calculated the need for invasive treatment of peri-implantitis in patient cohorts treated in a private specialist clinic. Surgical therapy and/or the use of systemic antibiotics were considered necessary in 11% to 67% of all patients, depending on the periodontal classification of the subjects. Data from the SSIA registry in Stockholm indicated that, while approximately 15,000 subjects received implants in Sweden annually over the last three years (2012-2014, Table 1), around 2,000 were, on an annual basis, treated surgically for peri-implantitis during the same time period (data from SSIA register, based on reimbursed surgeries with associated diagnosis of peri-implantitis). It may, again, be assumed that associated costs were high, and that consequences of peri-implantitis also, from a patient point of view, may be severe and, at times, dramatic.

[*Link to full study*](#)



Peri-implant mucositis treatments in humans: a systematic review

Blerina Zeza, DDS, MS and Andrea Pilloni, MD, DDS, MS

Ann Stomatol (Roma). 2012 Jul;3(3-4):83-9. Epub 2012 Jan 14.

Abstract

Aim

Peri-implant mucositis affects 39.4–80% of patients restored with dental implants. If left untreated it evolves in peri-implantitis. Thus far no predictable successful treatment has been reported for peri-implantitis, resulting in implant failure. Proper diagnosis and treatment of peri-implant mucositis is of crucial importance. This study aims to provide a comprehensive review of the available data regarding the effectiveness of peri-implant mucositis treatments in humans, parameters used for the diagnosis and treatment effect evaluation.

Materials and methods

A literature search for RCT and observational studies on peri-implant mucositis treatments in humans was conducted on Pubmed up to January 2012. CONSORT/STROBE and PRISMA checklists guided the evaluation of studies found and the writing of this review, respectively.

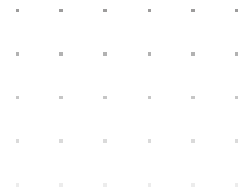
Results

Only 5 studies fulfilled the selection criteria. Few possibly effective treatments were studied. Diagnostic parameters reported were clinical only, while treatment effect evaluation was based on clinical and microbiological changes, except for one study reporting biochemical analysis. An evident heterogeneity characterized the follow-up intervals and methods used for reporting parameters changes.

Conclusions

Neither of studied treatments gave complete resolution of peri-implant mucositis. Different treatment strategies need to be studied. Authors suggest guidelines for a protocol of parameters used for determining the sample size, diagnosis and treatment effect, as well as follow-up periods, in order to permit evidence and comparison of different treatments effectiveness.

Aim



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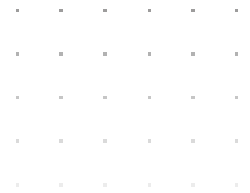
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Link to the full article: <http://www.ncbi.nlm.nih.gov/pmc/articles/PMC3555467/>



Interventions for replacing missing teeth: treatment of peri-implantitis.

[Esposito M1](#), [Grusovin MG](#), [Worthington HV](#).

Cochrane Database Syst Rev. 2012 Jan 18;1:CD004970. doi: 10.1002/14651858.CD004970.pub5.

Abstract

BACKGROUND:

One of the key factors for the long-term success of oral implants is the maintenance of healthy tissues around them. Bacterial plaque accumulation induces inflammatory changes in the soft tissues surrounding oral implants and it may lead to their progressive destruction (peri-implantitis) and ultimately to implant failure. Different treatment strategies for peri-implantitis have been suggested, however it is unclear which are the most effective.

OBJECTIVES:

To identify the most effective interventions for treating peri-implantitis around osseointegrated dental implants.

SEARCH METHODS:

We searched the Cochrane Oral Health Group's Trials Register, CENTRAL, MEDLINE and EMBASE. Hand searching included several dental journals. We checked the bibliographies of the identified randomised controlled trials (RCTs) and relevant review articles for studies outside the hand searched journals. We wrote to authors of all identified RCTs, to more than 55 dental implant manufacturers and an Internet discussion group to find unpublished or ongoing RCTs. No language restrictions were applied. The last electronic search was conducted on 9 June 2011.

SELECTION CRITERIA:

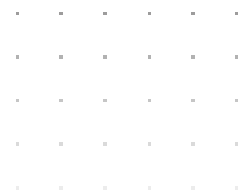
All RCTs comparing agents or interventions for treating peri-implantitis around dental implants.

DATA COLLECTION AND ANALYSIS:

Screening of eligible studies, assessment of the methodological quality of the trials and data extraction were conducted in duplicate and independently by two review authors. We contacted the authors for missing information. Results were expressed as random-effects models using mean differences for continuous outcomes and risk ratios for dichotomous outcomes with 95% confidence intervals (CI). Heterogeneity was to be investigated including both clinical and methodological factors.

MAIN RESULTS:

Fifteen eligible trials were identified, but six were excluded. The following interventions were compared in the nine included studies: different non-surgical interventions (five trials); adjunctive treatments to non-surgical interventions (one trial); different surgical interventions (two trials);

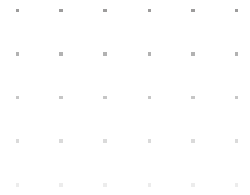


adjunctive treatments to surgical interventions (one trial). Follow-up ranged from 3 months to 4 years. No study was judged to be at low risk of bias. Statistically significant differences were observed in two small single trials judged to be at unclear or high risk of bias. After 4 months, adjunctive local antibiotics to manual debridement in patients who lost at least 50% of the bone around implants showed improved mean probing attachment levels (PAL) of 0.61 mm (95% confidence interval (CI) 0.40 to 0.82) and reduced probing pockets depths (PPD) of 0.59 mm (95% CI 0.39 to 0.79). After 4 years, patients with peri-implant infrabony defects > 3 mm treated with Bio-Oss and resorbable barriers gained 1.4 mm more PAL (95% CI 0.24 to 2.56) and 1.4 mm PPD (95% CI 0.81 to 1.99) than patients treated with a nano crystalline hydroxyapatite.

AUTHORS' CONCLUSIONS:

There is no reliable evidence suggesting which could be the most effective interventions for treating peri-implantitis. This is not to say that currently used interventions are not effective. A single small trial at unclear risk of bias showed the use of local antibiotics in addition to manual subgingival debridement was associated with a 0.6 mm additional improvement for PAL and PPD over a 4-month period in patients affected by severe forms of peri-implantitis. Another small single trial at high risk of bias showed that after 4 years, improved PAL and PPD of about 1.4 mm were obtained when using Bio-Oss with resorbable barriers compared to a nano crystalline hydroxyapatite in peri-implant infrabony defects. There is no evidence from four trials that the more complex and expensive therapies were more beneficial than the control therapies which basically consisted of simple subgingival mechanical debridement. Follow-up longer than 1 year suggested recurrence of peri-implantitis in up to 100% of the treated cases for some of the tested interventions. As this can be a chronic disease, re-treatment may be necessary. Larger well-designed RCTs with follow-up longer than 1 year are needed.

Comment in: [No reliable evidence suggesting what is the most effective interventions for treating peri-implantitis](#). [Evid Based Dent. 2012]



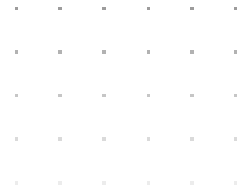
Treatment Alternatives to Negotiate Peri-Implantitis

Eli E. Machtei *

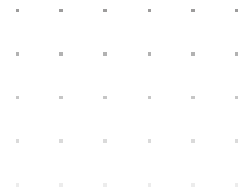
Advances in Medicine Volume 2014 (2014), Article ID 487903,

Abstract

Peri-implant diseases are becoming a major health issue in dentistry. Despite the magnitude of this problem and the potential grave consequences, commonly acceptable treatment protocols are missing. Hence, the present paper reviews the literature treatment of peri-implantitis in order to explore their benefits and limitations. Treatment of peri-implantitis may include surgical and nonsurgical approaches, either individually or combined. Nonsurgical therapy is aimed at removing local irritants from the implants' surface with or without surface decontamination and possibly some additional adjunctive therapies agents or devices. Systemic antibiotics may also be incorporated. Surgical therapy is aimed at removing any residual subgingival deposits and additionally reducing the peri-implant pockets depth. This can be done alone or in conjunction with either osseous respective approach or regenerative approach. Finally, if all fails, explantation might be the best alternative in order to arrest the destruction of the osseous structure around the implant, thus preserving whatever is left in this site for future reconstruction. The available literature is still lacking with large heterogeneity in the clinical response thus suggesting possible underlying predisposing conditions that are not all clear to us. Therefore, at present time treatment of peri-implantitis should be considered possible but not necessarily predictable. Peri-implant diseases are becoming a major health issue in dentistry. Despite the magnitude of this problem and the potential grave consequences, commonly acceptable treatment protocols are missing. Hence, the present paper reviews the literature treatment of peri-implantitis in order to explore their benefits and limitations. Treatment of peri-implantitis may include surgical and nonsurgical approaches, either individually or combined. Nonsurgical therapy is aimed at removing local irritants from the implants' surface with or without surface decontamination and possibly some additional adjunctive therapies agents or devices. Systemic antibiotics may also be incorporated. Surgical therapy is aimed at removing any residual subgingival deposits and additionally reducing the peri-implant pockets depth. This can be done alone or in conjunction with either osseous respective approach or regenerative approach. Finally, if all fails, explantation might be the best alternative in order to arrest the destruction of the osseous structure around the implant, thus preserving whatever is left in this site for future reconstruction. The available literature is still lacking with large heterogeneity in the clinical response thus suggesting possible underlying predisposing conditions that are not all clear to us. Therefore, at present time treatment of peri-implantitis should be considered possible but not necessarily predictable.



Link to the full article: <http://www.ncbi.nlm.nih.gov/pmc/articles/PMC4590969/>



Anti-infective surgical therapy of peri-implantitis. A 12-month prospective clinical study.

Heitz-Mayfield LJ¹, Salvi GE, Mombelli A, Faddy M, Lang NP; Implant Complication Research Group.

Clin Oral Implants Res. 2012 Feb;23(2):205-10. doi: 10.1111/j.1600-0501.2011.02276.x. Epub 2011 Aug 9.

Abstract

AIM:

The aim of this prospective cohort study was to evaluate an anti-infective surgical protocol for the treatment of peri-implantitis.

MATERIALS AND METHODS:

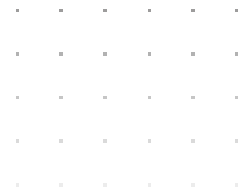
Thirty-six implants in 24 partially dentate patients with moderate to advanced peri-implantitis were treated using an anti-infective surgical protocol incorporating open flap debridement and implant surface decontamination, with adjunctive systemic amoxicillin and metronidazole. Treatment outcomes were assessed at 3, 6 and 12 months. Patient-based statistical analyses using multiple regression analyses were performed.

RESULTS:

There was 100% survival of treated implants at 12 months. At 3 months, there were statistically significant ($P < 0.01$) reductions in mean probing depths (PD), Bleeding on Probing (BoP) and suppuration. The greater the mean PD at baseline, the greater the PD reduction at 3 months. At 3 months, there was also a significant mean facial mucosal recession of 1 mm ($P < 0.001$). All these changes were maintained at 6 and 12 months. At 12 months, all treated implants had a mean PD < 5 mm, while 47% of the implants had complete resolution of inflammation (BoP negative). At 12 months, 92% of implants had stable crestal bone levels or bone gain. There were no significant effects of smoking on any of the treatment outcomes.

CONCLUSIONS:

For the treatment of peri-implantitis, an anti-infective protocol incorporating surgical access, implant surface decontamination and systemic antimicrobials followed by a strict postoperative protocol was effective at 3 months with the results maintained for up to 12 months after treatment.



Surgical Treatment of Peri-implantitis: Treatment Results -a pilot study

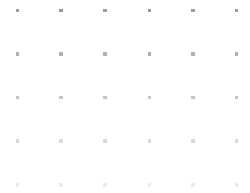
Lina Bengtzboe Stina Öskog

Not yet published

Abstract

Peri-implantitis is an infectious disease and one of the treatment methods involves surgical debridement of the infected area. The aim of this pilot study was to investigate treatment outcome after surgical treatment of peri-implantitis in humans. Outcome measures were reduction in pocket probing depth (PPD) and bleeding on probing and/or suppuration (BOP/Sup). Eight patients, with a total amount of 28 implants, who were diagnosed with peri-implantitis were surgically treated with a non regenerative surgical method including debridement and removal of granulation tissue combined with osteoplasty. Oral hygiene instructions were given and after 6 to 18 months a clinical reexamination was performed by two dental students at Umeå University. PPD and BOP/Sup data at the re-examination were retrospectively compared to baseline data. The results of the study showed a reduction in mean PPD and BOP/Sup after surgery at patient level. A significant reduction in mean PPD was shown ($p > 0.05$), while the reduction in BOP/Sup was not significant. At patient level, the mean reduction in mean PPD was 1.6 mm and in BOP/Sup 26%. Results varied among patients, suggesting that treatment outcome is influenced by several different factors. Tendencies that risk factors such as smoking and poor oral hygiene may have affected the treatment result were noted. In conclusion, our study shows that surgical therapy may be a beneficial treatment method for peri-implantitis in terms of reduction of PPD and BOP/Sup.

[Link to full study](#)



Management of peri-implantitis

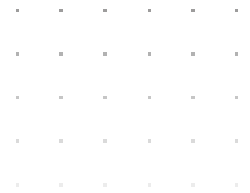
Jayachandran Prathapachandran¹ and Neethu Suresh¹

Dent Res J (Isfahan). 2012 Sep-Oct; 9(5): 516–521.

Abstract

Peri-implantitis is a site-specific infectious disease that causes an inflammatory process in soft tissues, and bone loss around an osseointegrated implant in function. The etiology of the implant infection is conditioned by the status of the tissue surrounding the implant, implant design, degree of roughness, external morphology, and excessive mechanical load. The microorganisms most commonly associated with implant failure are spirochetes and mobile forms of Gram-negative anaerobes, unless the origin is the result of simple mechanical overload. Diagnosis is based on changes of color in the gingiva, bleeding and probing depth of peri-implant pockets, suppuration, X-ray, and gradual loss of bone height around the tooth. Treatment will differ depending upon whether it is a case of peri-implant mucositis or peri-implantitis. The management of implant infection should be focused on the control of infection, the detoxification of the implant surface, and regeneration of the alveolar bone. This review article deals with the various treatment options in the management of peri-implantitis. The article also gives a brief description of the etiopathogenesis, clinical features, and diagnosis of peri-implantitis.

Link to the full article: <http://www.ncbi.nlm.nih.gov/pmc/articles/PMC3612185/>



The Therapy of Peri-implantitis: A Systematic Review

Lisa J. A. Heitz-Mayfield, BDS, MDS, Odont Dr1/Andrea Mombelli, Prof Dr Med Dent2A

Int J Oral Maxillofac Implants 2014;29(Suppl):325–345. doi: 10.11607/jomi.2014suppl.g5.3

Abstract

PURPOSE.

To evaluate the success of treatments aimed at the resolution of peri-implantitis in patients with osseointegrated implants.

MATERIALS AND METHODS

The potentially relevant literature was assessed independently by two reviewers to identify case series and comparative studies describing the treatment of peri-implantitis with a follow-up of at least 3 months. Medline, Embase, and The Cochrane Library were searched. For the purposes of this review, a composite criterion for successful treatment outcome was used which comprised implant survival with mean probing depth < 5 mm and no further bone loss.

RESULTS

A total of 43 publications were included: 4 papers describing 3 nonsurgical case series, 13 papers describing

10 comparative studies of nonsurgical interventions, 15 papers describing 14 surgical case series, and 11

papers describing 6 comparative studies of surgical interventions. No trials comparing nonsurgical with

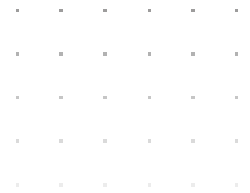
surgical interventions were found. The length of follow-up varied from 3 months to 7.5 years. Due to the

heterogeneity of study designs, peri-implantitis case definitions, outcome variables, and reporting, no meta analysis

was performed. Eleven studies could be evaluated according to a composite success criterion.

Successful treatment outcomes at 12 months were reported in 0% to 100% of patients treated in 9 studies

and in 75% to 93% of implants treated in 2 studies. Commonalities in treatment approaches between



studies included (1) a pretreatment phase, (2) cause-related therapy, and (3) a maintenance care phase.

CONCLUSIONS

While the available evidence does not allow any specific recommendations for the therapy of peri-implantitis, successful treatment outcomes at 12 months were reported in a majority of patients in 7

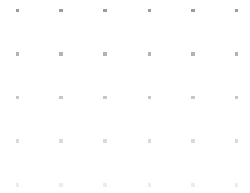
studies. Although favorable short-term outcomes were reported in many studies, lack of disease resolution

as well as progression or recurrence of disease and implant loss despite treatment were also reported. The

reported outcomes must be viewed in the context of the varied peri-implantitis case definitions and severity

of disease included as well as the heterogeneity in study design, length of follow-up, and exclusion/inclusion

[Link to the full study](#)



FOLLOW-UP STUDY OF PERI-IMPLANTITIS CASES AFTER TREATMENT

Georgios Charalampakis¹, Per Rabe², Åsa Leonhardt^{1,3} and Gunnar Dahlén¹

J Clin Periodontol 2011; doi: 10.1111/j.1600-051X.2011.01759.x.

Abstract

AIM

The aim of this retrospective study was to follow patient cases in a longitudinal manner after peri-implantitis treatment.

MATERIALS AND METHODS

Two hundred and eighty-one patient cases were selected consecutively from the archives of the Oral Microbiological Diagnostic Laboratory, Gothenburg, Sweden based on microbial analysis of bacterial samples taken from diseased implants. It was feasible to follow-up 245 patients after treatment for a period ranging from 9 months to 13 years.

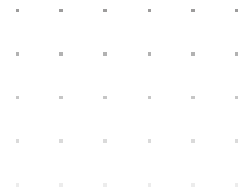
RESULTS

In 54.7% of the patients it was not feasible to arrest progression of peri-implantitis. Smoking and smoking dose were found to be significantly correlated to failure of peri-implantitis treatment ($p < 0.05$). Early disease development was also significantly associated with failure ($p < 0.05$). Bone plasty in conjunction to antibiotics during surgery was significantly associated with arrested lesions ($p < 0.05$). In a multiple regression model disease development was the only independent variable to significantly predict the likelihood of treatment success.

CONCLUSIONS

Peri-implant health may not be easy to establish, especially in cases that develop disease early. Homogenous treatment protocols rather than empirical treatment attempts should be adopted.

[Link to the full study](#)



Detoxification of Implant Surfaces Affected by Peri-Implant Disease: An Overview of Surgical Methods

Pilar Valderrama¹ and Thomas G. Wilson Jr²

Open Dent J. 2014 May 16;8:77-84. doi: 10.2174/1874210601408010077. eCollection 2014.

Abstract

PURPOSE.

Peri-implantitis is one of the major causes of implant failure. The detoxification of the implant surface is necessary to obtain re-osseointegration. The aim of this review was to summarize in vitro and in vivo studies as well as clinical trials that have evaluated surgical approaches for detoxification of the implant body surfaces.

MATERIALS AND METHODS

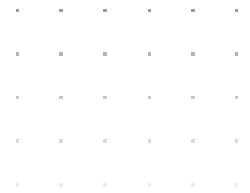
A literature search was conducted using MEDLINE (PubMed) from 1966 to 2013. The outcome variables were the ability of the therapeutic method to eliminate the biofilm and endotoxins from the implant surface, the changes in clinical parameters, radiographic bone fill, and histological re-osseointegration. Results. From 574 articles found, 76 were analyzed. The findings, advantages, and disadvantages of using mechanical, chemical methods and lasers are discussed.

CONCLUSIONS

Complete elimination of the biofilms is difficult to achieve. All therapies induce changes of the chemical and physical properties of the implant surface. Partial re-osseointegration after detoxification has been reported in animals. Combination protocols for surgical treatment of peri-implantitis in humans have shown some positive clinical and radiographic results, but long-term evaluation to evaluate the validity and reliability of the techniques is needed.

Discussion

As more dental implants are placed and remain in function for longer periods the prevalence of peri-implant diseases increases. From this overview of the available literature, it can be said that no reliable and valid therapy can be made based on the published articles available and that the

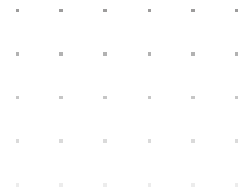


accuracy of the data varies. This agrees with the results of network meta-analysis [6] and systematic reviews [78, 79]. Most of the human studies published are cases series with follow-up periods ranging from 6 months to 24 months making it difficult to determine the stability of the newly formed tissues over time. In the present review it was found that most of the studies do not report rates of implant failures but other surrogate measurements like probing depths or clinical attachment levels. Therefore it is difficult to determine what approach will improve implant survival. This is in agreement with data reported by Faggion Jr. [80, 81].

It can also be stated that presently reattachment of bone to previously diseased implant surfaces is at best unpredictable. Histologic proof of re-osseointegration to previously contaminated implant surfaces in humans was not found. At present a combination of physical and chemical approaches possibly with appropriate laser therapy may prove to provide more predictable results. It should be noted that the profession is early in its understanding of these diseases and their treatment.

It can be stated with some assurance that physical alteration (smoothing) of the implant surface using metallic instruments has been demonstrated to slow or halt the progression of bone loss in humans as well as animals. While this application is certainly useful, the drawbacks include soft tissue retraction and esthetic compromises. From this review it can be argued that further investigation of optimal ways to treat implants affected by peri-implantitis and peri-implant mucositis as well as the prevention of these problems is warranted.

Link to the full article: <http://www.hindawi.com/journals/ijid/2013/740680/>



Comparison of the thermal and surface changes of dental implant using rotary instruments and piezoelectric device after implantoplasty: an in vitro study

1 Saeed Raoofi *2 Mehrnoosh Sabzeghabaie 3 Reza Amid

Journal of Dental School 2013; 31(4): 191-202

Abstract

PURPOSE.

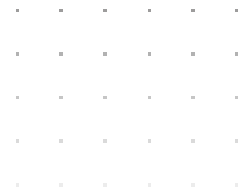
Peri-implantitis is an irreversible inflammatory reaction in the soft and hard tissues around a functional implant. One of the treatment approaches of this disease include smoothing and polishing the rough surface and removing threads on the implants using rotary instruments, which is called implantoplasty. Clinicians should perform implantoplasty with caution because it may raise the temperature of the implant body as well as the surrounding bone. This study aimed to compare micromorphology and thermal changes obtained with different rotary instruments and piezoelectric device after implantoplasty.

METHODS

In this in vitro study 48 Intra Lock fixture surfaces were processed in 60 seconds with six polishing procedures using 6,12 bladed carbide burs, 90, 30 µm mean-particles-size diamond burs, and piezosurgery inserts OT1 (grain size= 91 µm) and OP5 (grain size= 30 µm). These instruments were applied in single or sequences procedures. Variations in temperature were recorded every 5 seconds. The roughness of treated surfaces was evaluated with a profilometer for Ra1, Rz1 (single polish procedures), Ra2, and Rz2 (sequence polish procedures) parameters. Also, surfaces were observed using a field emission scanning electron after each step of implantoplasty.

RESULTS

The piezosurgery group showed statistically significant differences with the other two groups (maximum temperature 1.2°C). No statistically significant differences were observed between the carbide and diamond burs regarding the temperature changes and the temperature decreased from the start point in both groups. The mean Ra value in piezoelectric group (1.53 (0.23)) was significantly lower than diamond (2.45 (0.40), $p < 0.05$) and carbide (2.10 (0.28), $p < 0.05$) groups. Besides, this measure in the carbide group was significantly lower than that of the diamond group ($p < 0.05$). Rz1 value was significantly greater in diamond and carbide groups compared to piezoelectric group. The results revealed significant differences among the three groups

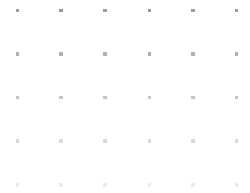


concerning Rz2. The minimum Rz2 value was seen in piezoelectric group, while the diamond group showed the highest Rz2 parameter.

CONCLUSIONS

This in vitro study showed that in suitable cooling conditions, implantoplasty with rotary and piezoelectric devices does not produce excessive heat increases which can damage the soft tissue or bone around the affected implant. The piezoelectric device produced smoother surfaces in single or sequence procedures compared to the burs and can be useful for implantoplasty.

Link to the full article: http://jds.sbm.ac.ir/files/site1/user_files_6197a6/admin-A-10-1-980-1dedfc9.pdf



Evaluation of an air-abrasive device with amino acid glycine-powder during surgical treatment of peri-implantitis.

Toma S, Lasserre JF, Taïeb J, Brex MC.

Quintessence Int. 2014 Mar;45(3):209-19. doi: 10.3290/j.qi.a31205.

Abstract

OBJECTIVE:

The aim of this retrospective study was to analyze collected data concerning the effect of an air-abrasive device (Perio-Flow®) during surgical treatment of peri-implantitis without addition of any antimicrobials.

METHOD AND MATERIALS:

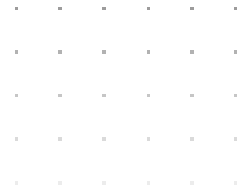
Data reports from 22 implants with peri-implantitis surgically treated using either an air-abrasive device (Perio-Flow) (test group), or plastic curettes and cotton pellets impregnated with saline (control group) were analyzed for the present study. Clinical and radiographic parameters plaque index (PI), gingival index (GI), probing pocket depth (PPD), and bone loss (BL) were previously assessed at baseline, 6 months, and 12 months after treatment. A repeated measures ANOVA test was used for each clinical and radiographic parameter (PI, GI, PPD, and BL). The implant and the patient were considered separately as the statistical unit.

RESULTS:

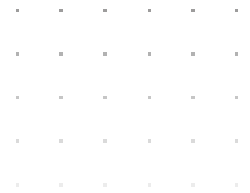
Regarding between group comparisons, PI scores remained low during the entire study period (at implant and patient levels). At the end of the study, GI and PPD reductions were statistically higher ($P < .05$) in the Perio-Flow group (implant level), and no differences were observed between the two groups at patient level ($P > .05$) (repeated measures ANOVA test). It was also noted that BL analyses (implant and patient levels) revealed no differences between baseline and 12 months in both groups. Nevertheless, only 8% from each treatment group were considered stabilized after 12 months.

CONCLUSION:

Within the limitations of the present study, both groups (Perio-Flow and its control group) revealed a significant reduction of the clinical parameters. Moreover, the air-abrasive device group yielded better improvements regarding GI and PPD when the implant was considered as the statistical unit. However, if the stabilization of the disease was the final objective, these two treatments failed in resolving its activity. A longer follow-up and a larger number of patients would be needed to



confirm these results and the benefit of adding this air-abrasive method of decontamination to the surgical procedure.



Bactericidal activity of phosphoric acid, citric acid, and EDTA solutions against *Enterococcus faecalis*.

Arias-Moliz MT¹, Ferrer-Luque CM, Espigares-Rodríguez E, Liébana-Ureña J, Espigares-García M.

Oral Surg Oral Med Oral Pathol Oral Radiol Endod. 2008 Aug;106(2):e84-9. doi: 10.1016/j.tripleo.2008.04.002. Epub 2008 Jun 13.

Abstract

OBJECTIVES:

The objectives of this study were to evaluate the minimal bactericidal concentration (MBC) for *Enterococcus faecalis* of phosphoric acid, citric acid, and ethylene diamine tetra acetic acid (EDTA) solutions, and to determine the contact time required for 2.5% and 5% phosphoric acid, 10% and 25% citric acid, and 17% EDTA to exert bactericidal activity.

STUDY DESIGN:

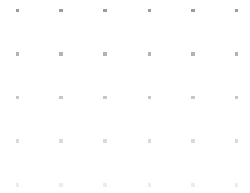
Bactericidal activity was tested by means of the dilution neutralization method in accordance with BS-EN-1040:2005 norm, using contact times of 0.5 to 60 minutes.

RESULTS:

The MBCs of citric and phosphoric acid were 20% and 2.5%, respectively. EDTA solution lacks bactericidal activity, even after 60 minutes of contact. The 2.5% and 5% phosphoric acid solutions required 5- and 3-minute contact times, and the 10% and 25% citric acid solutions required 10- and 3-minute contact times, respectively.

CONCLUSIONS:

Phosphoric acid revealed bactericidal activity against *E. faecalis* and required less time than citric acid to exert its activity.



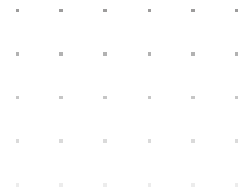
Hyaluronic acid-based hydrogels functionalized with heparin that support controlled release of bioactive BMP-2

[Gajadhar Bhakta,^a](#) [Bina Rai,^a](#) [Zophia X.H. Lim,^a](#) [James H. Hui,^b](#) [Gary S. Stein,^c](#) [Andre J. van Wijnen,^c](#) [Victor Nurcombe,^a](#) [Glenn D. Prestwich,^d](#) and [Simon M. Coola,^{b,*}](#)

Biomaterials. 2012 Sep;33(26):6113-22. doi: 10.1016/j.biomaterials.2012.05.030. Epub 2012 Jun 9.

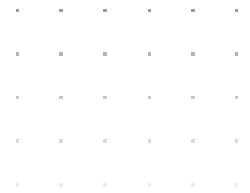
Abstract

Bone morphogenetic protein-2 (BMP-2) is a potent osteoinductive factor, yet its clinical use is limited by a short biological half-life, rapid local clearance and propensity for side effects. Heparin (HP), a highly sulfated glycosaminoglycan (GAG) that avidly binds BMP-2, has inherent biological properties that may circumvent these limitations. Here, we compared hyaluronan-based hydrogels formulated to include heparin (Heprasil™) with similar gels without heparin (Glycosil™) for their ability to deliver bioactive BMP-2 in vitro and in vivo. The osteogenic activity of BMP-2 released from the hydrogels was evaluated by monitoring alkaline phosphatase (ALP) activity and SMAD 1/5/8 phosphorylation in mesenchymal precursor cells. The osteoinductive ability of these hydrogels was determined in a rat ectopic bone model by 2D radiography, 3D μ -CT and histological analyses at 8 weeks post-implantation. Both hydrogels sustain the release of BMP-2. Importantly, the inclusion of a small amount of heparin (0.3% w/w) attenuated release of BMP-2 and sustained its osteogenic activity for up to 28 days. In contrast, hydrogels lacking heparin released more BMP-2 initially but were unable to maintain BMP-2 activity at later time points. Ectopic bone-forming assays using transplanted hydrogels emphasized the therapeutic importance of the initial burst of BMP-2 rather than its long-term osteogenic activity. Thus, tuning the burst release phase of BMP-2 from hydrogels may be advantageous for optimal bone formation. Bone morphogenetic protein-2 (BMP-2) is a potent osteoinductive factor, yet its clinical use is limited by a short biological half-life, rapid local clearance and propensity for side effects. Heparin (HP), a highly sulfated glycosaminoglycan (GAG) that avidly binds BMP-2, has inherent biological properties that may circumvent these limitations. Here, we compared hyaluronan-based hydrogels formulated to include heparin (Heprasil™) with similar gels without heparin (Glycosil™) for their ability to deliver bioactive BMP-2 in vitro and in vivo. The osteogenic activity of BMP-2 released from the hydrogels was evaluated by monitoring alkaline phosphatase (ALP) activity and SMAD 1/5/8 phosphorylation in mesenchymal precursor cells. The osteoinductive ability of these hydrogels was determined in a rat ectopic bone model by 2D radiography, 3D μ -CT and histological analyses at 8 weeks post-implantation. Both hydrogels sustain the release of BMP-2. Importantly, the inclusion of a small amount of heparin (0.3% w/w) attenuated release of BMP-2 and sustained its osteogenic activity for up to 28 days. In contrast, hydrogels lacking heparin released more BMP-2 initially but were



unable to maintain BMP-2 activity at later time points. Ectopic bone-forming assays using transplanted hydrogels emphasized the therapeutic importance of the initial burst of BMP-2 rather than its long-term osteogenic activity. Thus, tuning the burst release phase of BMP-2 from hydrogels may be advantageous for optimal bone formation.

Link to the full article: <http://www.ncbi.nlm.nih.gov/pmc/articles/PMC3628623/>



Implant surgery: treatment with a fluid gel compound with hyaluronic acid and piperacillin plus tazobactam

Giacomo Bartoloni Saint Omer

Doctor Os, January 2015

Abstract

AIM

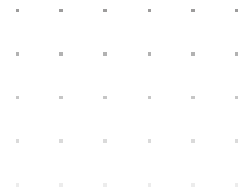
Evaluation of applicability, clinical benefits and tolerability of a biomaterial as an organic scaffold with hyaluronic acid and piperacillin + tazobactam used alone or in combination with bone allograft and resorbable collagen membrane in the restoration of bone defects as well as in prevention and treatment of peri-implant infections.

METHOD AND MATERIALS:

A group of 43 patients with peri-implantitis and peri-implant bone defects or requiring sinus lift and extractive surgery were treated using the product in addition to standard procedures, the product was also used to wash sockets and applied on the implant before its placement in order to prevent early infections.

RESULTS AND CONCLUSIONS

The results of this preliminary study on selected patients, showed a good applicability of the product in surgical cases, with higher benefits and an excellent clinical tolerability. The biomaterial helped the processes of tissue repair creating a favourable environment for healing through the prevention of bacterial infections, owing to the presence of piperacillin and tazobactam, an antibiotic with broad spectrum activity against Gram + and Gram



Results

The results of clinical assessment of signs and symptoms after 8 days were excellent in 51% of patients, good in 46% and poor in 3%. After 3-6 months, the results of clinic assessment were excellent in all the patients treated (Tab. 1).

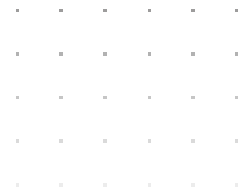
In the 37 patients belonging to the 5 groups listed in Table 1, no local or systemic side effects were recorded, with the exception of 4 patients (3 in the extractions group and 1 in the peri-implant defects group) who reported a “bad taste” on the first day after surgery.

Table 2 summarises the pre- and post-treatment data for the three groups of patients on whom at least one implant was inserted.

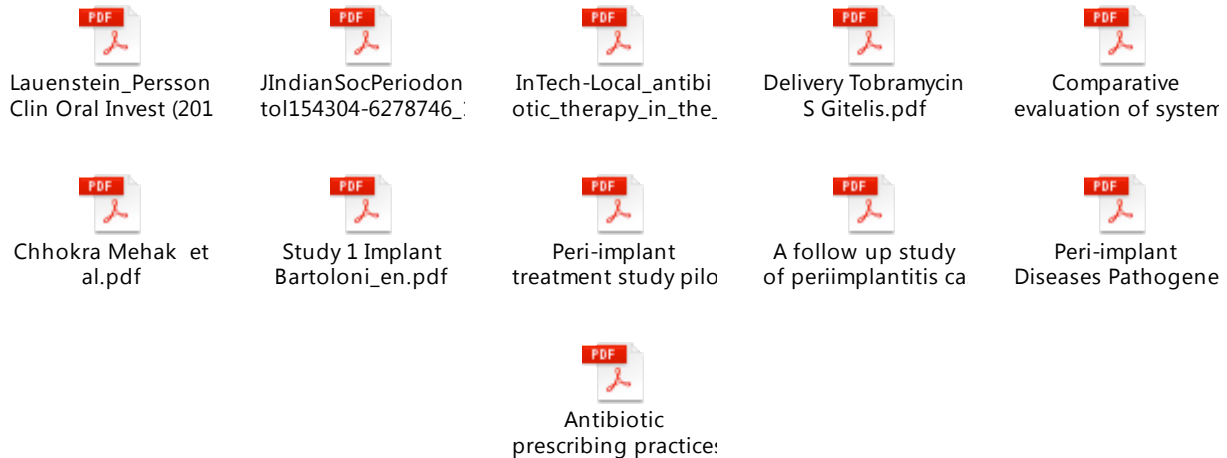
The group suffering from severe peri-implantitis consisted of 6 patients with 6 implants. Table 3 summarises the pre- and post-treatment changes in soft tissues, and Table 4 the radiographic variations in bone levels. The results for the 6 implants with severe peri-implantitis were a gain of bone tissue around the implant, which varied from 50 to 80% (Fig. 1).

No local or systemic side effects were detected.

[Link to the full study](#)



Full Studies and other additional information



Other useful books/articles/studies

Goodman and Gilman's : The pharmacological Basis of Therapeutics. Sixth Edition P. 1094

Lindhe J, Karring T, Lang NP. Clinical periodontology and Implant dentistry. 4th edi. Blackwell Munksgaard Oxford: 479-81

Mombelli, A.J. Van Winkelhoff, The systemic use of antibiotics in periodontal therapy

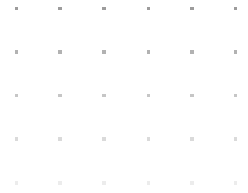
Peri-implant diseases: Consensus Report of the Sixth European Workshop on Periodontology. Authors: Jan Lindhe, Joerg Meyle, on behalf of Group D of the European Workshop on Periodontology (First published: 26 August 2008)

Schwarz & Becker. Quintessence Publishing Co. Ltd. London, 2010. Peri-implant Infection. Etiology, Diagnosis and Treatment.

Surgical decontamination protocol of peri-implantitis with the use of implantoplasty, guided bone regeneration and local administration of piperacillin /tazobactam. Giacomo Bartoloni Saint Omer, DD - Alessandro Tosetti, MD,DD

Zitzmann NU, Berglundh T. Definition and prevalence of peri-implant diseases . J Clin Periodontol. 2008;35(suppl 8):S286-S291.

<http://onlinelibrary.wiley.com/doi/10.1111/j.1834-7819.2009.01147.x/pdf>



<http://www.oralhealthgroup.com/features/peri-implantitis-treatment-options/?er=NA>

<http://www.sciencedirect.com/science/article/pii/S1687857414000365>