Title:

Influence of new implant surface decontamination method (Galvosurge®) in the surgical reconstructive treatment of peri-implant related intrabony defects. Randomized clinical trial.

Key words:

Reconstructive surgical therapy, peri-implantitis, peri-implant bone defects, bone graft

Background:

Periimplantitis is a pathological condition that occurs in the tissues surrounding dental implants. It is characterized by inflammation of the peri-implant connective tissue and loss of progressive support bone (1). In a recent systematic review, a 22% prevalence of peri-implantitis has been described (2). If the literature is analyzed, it can be verified how different percentages of prevalence are reported due to the different definition of this pathological condition depending on the study analyzed, being from 1% to 47% (3). In addition, it has been suggested that this bone loss is time-dependent and that the follow-up time of the different studies can also affect the percentage of prevalence described (4, 5)

The objective of the treatment of peri-implantitis is to resolve the inflammation of the soft tissues and stop the additional loss of the peri-implant support bone. Recent systematic reviews report that regardless of the non-surgical treatment modality used, it is insufficient to stop the disease (6), while surgical treatment has shown greater efficacy and in the longer term (7) (8). Furthermore, it is demonstrated that factors such as the implant surface decontamination method has a significant influence on the results of surgical treatment. Several implante surface decontamination methods have been proposed (curettes, titanium brushes, ultrasonic methods, glycine powder air-polishing…) but till date, none of them has shown superiority over the others (9-12). Decontamination methods should not only remove effectively the attached biofilm and calculus, but also avoid any significant deleterious changes at the implant surface in order to

perform the reconstructive surgery around the implant surface and promote the re-osseointegration.

Objective:

The overall objective of the present project is to evaluate the clinical efficacy of the new implant surface decontamination method called Galvosurge® in the treatment of peri-implant bone defects and arrest the progression of the peri-implant pathology. Therefore, the main objective is to assess the efficacy of the electrolytic method in cleaning the contaminated implant surface. Primary outcome is treatment success (absence of BoP/Pus, PPD ≤ 5mm and ≤ 1mm recession of mucosal margin). Secondary outcomes include, volumetric changes, radiographic defect fill, treatment complications appearance and patient-centered outcomes (PROM).

Rationale for the study:

There is no enough evidence to evaluate the clinical efficacy of this new implant surface decontamination method called Galvosurge® in the treatment of peri-implant related intrabony defects.

Hypothesis:

Galvosurge implant surface decontamination method has a better outcome in terms of remove effectively the attached biofilm and calculus from implant surface when comparing with titanium brush.

Relevance for clinical practice:

The results of this project will help to understand the use of this innovative implant surface decontamination method in the reconstructive surgical therapy of peri-implantitis-related bone defects.

Materials & Methods:

Study population, design and treatment procedures:

The project will be conducted as a two-armed randomized controlled clinical trial of 1-year duration in 2 clinical centers. 40 systemically healthy patients with implants ≥ 1 year in function and diagnosed with advanced peri-implantitis at ≥ 1 implants will be enrolled.

Inclusion criteria:

- Age ≥ 18 years
- Peri-implant bone defect ≥ 3mm assessed radiographically
- PPD ≥ 5mm combined with bleeding on probing or supuration
- Intra-surgically, bone defect must have at least a intraosseous component of 3mm and a width of no more than 4mm
- implants ≥ 1 year in function

Exclusion criteria:

- Treated for peri-implantitis during previous 6 months
- Intake of systemic or local antibiotics during previous 6 months
- Pregnant patients
- Systemically unhealthy patients
- Patients allergic to collagen

Surgical procedures:

Surgical procedures will be performed one month after non surgical periodontal treatment. The same day of surgical therapy an antibiotic will be administered during 7 days (amoxicillin 500mg / 7 days / 8hours). Full thickness flap will be elevated and infected tissues will be removed.

Implant surface decontamination will be performed with test (Galvosurge®) or control methods (titanium brush) randomly assigned. The intrabony defect will be filled with Xenogain Collagen® and Xenoprotect® resorbable membrane and the flaps will be sutured to their previous position. Sutures will be removed 2 weeks after surgical therapy. Clinical examinations will be performed at 4,12,24 and 48 weeks after surgical therapy. Maintenance therapy will be realized at 12, 24 and 48 weeks after therapy.

Clinical assessments:

One calibrated examiner will perform the assessments. The following variables will be assessed at four sites around the implant: Plaque, probing pocket depth (PPD), bleeding on probing (BoP), probing attachment level (PAL) recession (REC). Keratinized mucosa (KM) will be measured in the buccal aspect of each included implant

Surgical assessments:

One calibrated examiner will perform the assessment. Taking into account the Schwarz et al 2010 peri-implant defect classification, the defect configuration will be measured to understand how much impact does it have on clinical outcomes. Furthermore intrabony defect characteristics will be measured.

Treatment success:

Treatment success will be defined as the absence of BoP/Pus, PPD ≤5 mm and ≤1 mm recession.

Radiographic assessments:

Intra-oral radiographs will be obtained prior to surgery (baseline) and at 6- and 12-months re-examinations. Analysis of radiographs will be performed by a specialist. The examiner will be blinded to treatment procedures. The assessment will include defect fill in both follow up visits.

Volumetric changes:

Intra-oral scanning will be obtained prior to surgery (baseline) at 6 months and at 12-months re-examination. Analysis of STL archives will be performed by a specialist. The examiner will be blinded to treatment procedures. The assessment will include volumetric changes after matching the baseline intra-oral scanning, 6 months intra-oral scanning and 12-months intra-oral scanning.

Primary endpoint:

The primary outcome of the present study is a composite definition of successful treatment outcome defined as absence of bleeding or suppuration on probing, absence of peri-implant probing depth ≤5mm and mucosal recession ≤1mm

Secondary endpoints:

- radiographic filling of the defect: It will be measured with Image J Software
- Risk of appearance of complications: they will be measured with a questionnaire recording suppuration, membrane exposure or grafting material exposure and soft tissue dehiscence.
- Patient reported outcomes measurements: patient pain perception and general satisfaction with surgical procedure and final outcomes.
- Need for analgesia after surgery
- Intervention time
- Soft and hard tissue volumetric changes. It will be measured with an intraoral scanner and compared with implant planning software.
- Impact of defect configuration in treatment outcomes: defect will be classified and outcomes between groups will be compared.

Indication:

Peri-implant bone defect ≥ 3mm assessed radiographically, PPD ≥ 5mm combined with bleeding on probing or supuration and Intra-surgically, bone defect must have at least a intraosseous component of 3mm and a width of no more than 4mm

Power calculation:

According to Roos-Jansaker et al 2007 and Renvert et al 2018, it was identified that a mean filling of the defect of 1.5mm could be detected with a standard deviation of ± 1.2mm after surgical treatment of peri-implantitis with a bone graft. Including 20 patients for each group a statistical power of 93% would be reached.

Data analysis:

The statistical analysis will take into account all the data collected before, during and after the surgical intervention. A descriptive statistic of the data obtained in both groups will be carried out during the study. For the analytical statistics a Shapiro-Wilk normality test will be performed for the quantitative variables. The changes in the means obtained between the initial situation and 12 months of follow-up will be evaluated using a McNemar test. The patient is the unit of analysis. The data obtained will be analyzed through the SPSS SPSS Statistics Desktop program, V21.00 (SPSS Inc., Chicago, IL, USA

Schedule of investigational events:

The flow chart and time schedule presented below illustrate the overall organization of the study including the sequence of examinations:

1. Ethical approval of protocol by local ethics committee
2. Study announcement and patient recruitment
3. Screening and identification of subjects. It is estimated that it will take about 18 months to recruit the total number of patients required for the trial

4. Baseline clinical examination of implants selected for the study. Non surgical periodontal treatment. Photographs, data collection of clinical parameters and measurements. Patient perception with peri-implantitis diagnosis will be also collected prior to surgery.

5. Radiographic examination, cone beam computed tomography and intraoral volumetric scanning will we recorded prior to surgery (within 2 weeks)

6. Surgical therapy including test or control decontamination method and reconstructive procedures. Assessment of PROM, photographs, periapical radiography and surgery time will be recorded.

7. 2 weeks: suture removal. Assessment of PROM and photographs

8. 4 weeks: photographs

9. 12 weeks: photographs, professional supra-mucosal cleaning and reinforcement of oral hygiene.

10. 24 weeks: photographs, periapical radiography, collection of posible complications and professional supra-mucosal cleaning and reinforcement of oral hygiene.

11. 48 weeks: photographs, periapical radiography, collection of posible complications, cone beam computed tomography, intraoral volumetric scanning and professional supra-mucosal cleaning and reinforcement of oral hygiene.

Ethical considerations and institutional review:

The protocol is being reviewed by the local Ethics Committee of Basque Country and the study will be registered at isrctn.com.

Each patient will receive oral and written information about study purpose and design and they will have to sign a consent. Patients have to understand that their participation in the study is voluntary and they can leave it when they want. The study will be carried out following the recommendations of Helsinki declaration. All the included patients will receive surgical

treatment of peri-implantitis and any adverse reaction will be recorded during the follow-up visits.

1. Facilities and expertise:

Study team:

Principal investigator:

Alberto Ortiz-Vigón (Department of Periodontology, Periocentrum Bilbao) has extensive experience in the field of periodontology, implant dentistry and peri-implantitis clinical research

Study monitoring:

Erik Regidor (Department of Periodontology, Periocentrum Bilbao) has experience in monitoring randomized controlled clinical trials. He will attend all the study during the inclusion period as well as the follow-up period.

Clinical / practical work:

All investigators are trained researches and specialists in periodontics.
All of them have an extended experience in periodontology, implant dentistry and surgical treatment of peri-implantitis.

2. Organization:

The study will be organized and monitored from Periocentrum Bilbao:

Principal Investigator: Dr. Alberto Ortiz-Vigón (Periocentrum Bilbao, Bilbao, Spain)
Clinical Research Coordinator: Dr. Erik Regidor (Periocentrum Bilbao, Bilbao, Spain)

3. Infrastructure

Periocentrum Bilbao has extended experience in periodontology and clinical research.
Periocentrum Bilbao will be responsible of their data collection and when the study is finished, data analysis and interpretation will be made.

4. Economy

Periocentrum Bilbao will be responsible for the cost of the surgical treatment of each included patient and follow-up visits until the protocol is completed

5. References

1. Schwarz F, Derks J, Monje A, Wang HL. Peri-implantitis. J Periodontol. 2018;89 Suppl 1:S267-S90.
2. Derks J, Tomasi C. Peri-implant health and disease. A systematic review of current epidemiology. J Clin Periodontol. 2015;42 Suppl 16:S158-71.
3. Tomasi C, Derks J. Clinical research of peri-implant diseases--quality of reporting, case definitions and methods to study incidence, prevalence and risk factors of peri-implant diseases. J Clin Periodontol. 2012;39 Suppl 12:207-23.
4. Fransson C, Tomasi C, Pikner SS, Grondahl K, Wennstrom JL, Leyland AH, et al. Severity and pattern of peri-implantitis-associated bone loss. J Clin Periodontol. 2010;37(5):442-8.
5. Derks J, Schaller D, Hakansson J, Wennstrom JL, Tomasi C, Berglundh T. Peri-implantitis - onset and pattern of progression. J Clin Periodontol. 2016;43(4):383-8.
6. Faggion CM, Jr., Listl S, Fruhauf N, Chang HJ, Tu YK. A systematic review and Bayesian network meta-analysis of randomized clinical trials on non-surgical treatments for peri-implantitis. J Clin Periodontol. 2014;41(10):1015-25.

7. Romeo E, Lops D, Chiapasco M, Ghisolfi M, Vogel G. Therapy of peri-implantitis with resective surgery. A 3-year clinical trial on rough screw-shaped oral implants. Part II: radiographic outcome. Clin Oral Implants Res. 2007;18(2):179-87.

8. Carcuac O, Derks J, Abrahamsson I, Wennstrom JL, Petzold M, Berglundh T. Surgical treatment of peri-implantitis: 3-year results from a randomized controlled clinical trial. J Clin Periodontol. 2017;44(12):1294-303.

9. De Tapia B, Mozas C, Valles C, Nart J, Sanz M, Herrera D. (2019) Adjunctive effect of modifying the implant- supported prosthesis in the treatment of peri- implant mucositis. Journal of Clinical Periodontology 46, 1050- 1060.

10. El Chaar, E.; Almogahwi, M.; Abdalkader, K.; Alshehri, A.; Cruz, S. (2020) Decontamination of the Infected Implant Surface: A Scanning Electron Microscope Study. Int. J. Periodontics Restor. Dent. 40, 395–401.

11. Lollobrigida M, Fortunato L, Serafini G, Mazzucchi G, Bozzuto G, Molinari A, Serra E, Menchini F, Vozza I, De Biase A. (2020) The prevention of implant surface alterations in the treatment of peri-implantitis: Comparison of three different mechanical and physical treatments. Int. J. Environ. Res. Public Health, 17, 2624.

12. Matsubara VH, Leong BW, Leong MJL, Lawrence Z, Becker T, Quaranta A (2019) Cleaning potential of different air abrasive powders and their impact on implant surface roughness. Clin Implant Dent Relat Res 22:96–104.