A NEW IMPLANT-ABUTMENT CONNECTION FOR BACTERIAL MICROLEAKAGE PREVENTION: AN IN VITRO STUDY

L. TETTAMANTI¹, F. CURA², C. ANDRISANI³, M. ANDREASI BASSI⁴, J. SILVESTRE-RANGIL⁵, A. TAGLIABUE¹

¹ Department of Medicine and Surgery, University of Insubria, Varese, Italy
² Department of Experimental, Diagnostic and Specialty Medicine, University of Bologna, Bologna, Italy
³ Private Practice in Matera, Italy
⁴ Private Practice in Rome, Italy
⁵ Department of Estomatology, University of Valencia, Valencia, Spain

SUMMARY

Purpose. The aim of our study is to evaluate the ability of a new type of implant (Konus Implant System®, Industrie biomediche e farmaceutiche, Italy) to isolate the internal of an implant-abutment connection from the external environment.

Materials and methods. To identify the capability of the implant to protect the internal space from the external environment, the passage of genetically modified Escherichia coli across implant-abutment interface was evaluated. Implants were immerged in a bacterial culture for twenty-four hours and then bacteria amount was measured inside implant-abutment interface with Real-time PCR.

Results. Bacteria were detected inside all studied implants, with a median percentage of 18% for Porphyromonas Gingivalis and 19% for Tannerella Forsythia.

Conclusion. The reported results are similar to previous work. Konus Implant System® showed bacterial leakage similar respect others implant systems (18% Porphyromonas Gingivalis, 19% Tannerella Forsytia versus 20% of Bicon® and Ankylos® systems). In spite of the limits of our study, none two-piece implant system has been demonstrated to perfectly close the gap between implant and abutment.

Key words: implant-abutment connection, implant dentistry, bacterial leakage, perimplantitis, bone resorption.

Introduction

Two-piece implant systems (TPISs) are used for oral rehabilitation both for fixed and removable prostheses (1-48). Bacterial loading can prevent osseointegration of a TPIS during the healing phase of the surgical intervention and, if uncontrolled, can cause peri-implantitis.

The time period for bacterial contamination of a TPIS after surgery can run from 14 days after exposure to the oral cavity to 2 or 3 months (49). Infection of implant surface of a TPIS may develop even during the surgical implant installation and proceed during the prosthetic phase. In a TPIS, the positioning of the implant-abutment connection in the supracrestal bone is important, in fact, screw loosening would allow bacterial leakage into the implant-abutment connection. It is accepted that the connection between implants and abutments in a TPIS exhibits
gaps where bacterial loading can grow and cause peri-implant tissue inflammation. To quantify microbial colonization in the implant-abutment connection the method most often used is Real-time Polymerase Chain Reaction (RT-PCR).

Konus Implant System®

Development and engineering of the Konus Implant System® (Industrie biomediche e farmaceutiche, Italy) includes the broadest selection of prosthetic components on the today’s market. All components are optimally suited and matched to the Konus Implant System® and allow for a large variety of dental treatment possibilities. The Konus Implant System® components and implant system assure for the best possible clinical and aesthetic results. The special external hex connection allows for a tight connection and allows for 360° placement of the prosthetics. The external hex interface is the most established connection system on the market, and the preferred choice for many training institutions and top-end users. Many clinicians worldwide continue to prefer the external hex for its ease of use, widespread availability, long history of clinical success, and from mere personal preference. It is also known to be more “forgiving” in situations of impassive fit or implant divergence. Konus Implant System® has therefore continued to refine its external hex range, to provide its loyal supporters with exceptional reliability alongside proven modern features. When completed an Konus implant/abutment connection is like a one-piece implant.

Konus Implant System® Connection

The development of external hex connections in implant dentistry has been reached and described in literature and publications. The Konus Implant System® connects the implant and abutment and gives an optimal load dispersion of the abutment into the implant. This allows for optimal product characteristics. The connection of the Konus Implant System® is so precise, that with 3 mm diameter implants allows for optimal restorations and chewing abilities. Also the bacterial seal and micro-free movement connection assure optimal aesthetic results and avoid bone and papilla-loss. In today’s implantology the usage of TPISs is more prominent than one-piece implants. This is due to clinical and prosthetic advantages with TPISs. By usage of TPISs, the peri-implant bone height is dependent upon which implant system is used. The influence of the peri-implant bone height is dependent from the mechanical and microbiological aspects of the abutment/implant connection. Through the mechanical connection and precision of this connection, screw loosening and eventually fractures in the area of the implant/abutment connection can be prevented. The micro-movement of the implant/abutment connection and the increasing micro-gap has been studied and verified by many clinicians. Zipprich et al. demonstrated bacterial leakage by simulating chewing with an X-ray video recording (50). Implant systems with an external hex should no present significant gaps or bacterial influence. In today’s clinical practice we find extreme variances and differences of implant and abutment connections.

Aim

The aim of our study is to evaluate ability of a new type of implant (Konus Implant System®, Industrie biomediche e farmaceutiche, Italy) to isolate the internal of an implant-abutment connection from the external environment.
Materials and methods

Implant preparation

In order to size up the ability of the implant to isolate the heart of the device from the external environment, we evaluated the passage of modified E. coli across the joint of the implant. The peculiarity of these bacteria is that they contain synthetic DNA target sequences in their plasmid. In detail, the plasmid contains two-sequence specific for two bacterial species (P. gingivalis and T. forsythia) and two genes for antibiotic selection (Kanamycin and Ampicillin). Bacteria were cultured in lysogeny broth (LB) containing both Kanamycin and Ampicillin (at a final concentration of 50ug/ml) at 37°C for 12-18h in a shaking incubator. Four Konus Implants System® (Konus Implants®, Industrie farmaceutiche e biomediche, Italy) were used in this study. Few microliters of LB with antibiotics were put inside the implants. The implants and the abutment are screwed with a force of 35 Newton. Few microliters of this culture were used to “contaminate” fresh LB with antibiotics contained in a micro centrifuge tube together with the implant. Tubes were then let at 37°C for 48h in a heater, in order to allow bacterial growth and their hypothetical passage within the implant. Inside the implant, instead, we just put LB and antibiotics without bacteria. To be sure that there were no contaminations, a negative control containing only LB and antibiotics, was prepared. Forty-eight hours later, implants were opened and samples were collected by dipping a paper probe in both the sites containing LB (external and internal to the implant) for each implant, and in the negative control too.

DNA extraction

Once collected, paper probe were put on a new micro centrifuge tube and processed for bacterial DNA extraction, by using the GenElute™ Bacterial Genomic DNA Kit (Sigma-Aldrich, St., St. Louis, MO, USA), following the manufacturing procedures. Briefly, samples were incubated with lysozyme and, subsequently with proteinase K to isolate DNA. Once extracted, DNA was purified by spin-column method.

Real-time polymerase chain reaction

Bacterial quantification was performed by Real-Time Polymerase Chain Reaction using the absolute quantification with the standard curve method. Primers and probes oligonucleotides for P. gingivalis and T. forsythia were designed basing on 16S rRNA gene sequences of the Human Oral Microbiome Database (HOMD 16S rRNA Ref-Seq Version 10.1). For the quantitative analysis, plasmid (Eurofin MWG Operon, Ebersberg Germany) containing the specific DNA target sequence was employed as standard. All reactions were performed in duplex, in 20ul final volumes; with 2X TaqMan Universal PCR master mix (Applied Biosystems, Foster City, CA, USA) and 50nM concentration of each primers and 200nM of the probes. Amplifications were carried out by using the ABI PRISM 7500 (Applied Bio systems, Foster City, CA, USA).

Statistical analysis

To evaluate if the difference in viability among outside and inside the implant was statistically significant, we applied Student’s t-test on average bacteria quantification at each time point.
Results

Bacteria quantification is reported in Table 1. In all the tested implants, bacteria were found in the inner side, with a median percentage of 18% for Porphyromonas Gingivalis and 19% for Tannerella Forsythia.

The analysis revealed that in both cases (internally and externally), bacteria grew for the first 48 hours but subsequently they started to dye, probably as a consequence of nutrient consumption.

| Implant | Bacteria | Bacteria quantity | Implant | Bacteria | Bacteria quantity | Passage of bacteria from outside to inside the implant (%) |
|---------|----------|-------------------|---------|----------|-------------------|-----------------------------------------------------------|
| 1       | P. gingivalis | 3671646          | 1       | P. gingivalis | 548110 | 14%                      |
|         | T. forsythia  | 3482534          |         | T. forsythia  | 519839 | 14%                      |
| 2       | P. gingivalis | 3590985          | 2       | P. gingivalis | 774478 | 21%                      |
|         | T. forsythia  | 5829062          |         | T. forsythia  | 1631951 | 27%                      |
| 3       | P. gingivalis | 5042971          | 3       | P. gingivalis | 1350469 | 26%                      |
|         | T. forsythia  | 5014941          |         | T. forsythia  | 1203405 | 23%                      |
| 4       | P. gingivalis | 4023610          | 4       | P. gingivalis | 352157 | 8%                       |
|         | T. forsythia  | 4078895          |         | T. forsythia  | 339744 | 8%                       |
| 5       | P. gingivalis | 2493735          | 5       | P. gingivalis | 789779 | 31%                      |
|         | T. forsythia  | 2414858          |         | T. forsythia  | 793444 | 32%                      |
| 6       | P. gingivalis | 1791008          | 6       | P. gingivalis | 518165 | 28%                      |
|         | T. forsythia  | 1750573          |         | T. forsythia  | 509566 | 29%                      |
| 7       | P. gingivalis | 2991545          | 7       | P. gingivalis | 536357 | 17%                      |
|         | T. forsythia  | 3008513          |         | T. forsythia  | 552056 | 18%                      |
| 8       | P. gingivalis | 1976481          | 8       | P. gingivalis | 385105 | 19%                      |
|         | T. forsythia  | 1893747          |         | T. forsythia  | 369124 | 19%                      |
| 9       | P. gingivalis | 2161590          | 9       | P. gingivalis | 856245 | 39%                      |
|         | T. forsythia  | 2081358          |         | T. forsythia  | 745513 | 35%                      |
| 10      | P. gingivalis | 7197591          | 10      | P. gingivalis | 630184 | 8%                       |
|         | T. forsythia  | 6960251          |         | T. forsythia  | 621550 | 8%                       |
| 11      | P. gingivalis | 2293864          | 11      | P. gingivalis | 102427 | 4%                       |
|         | T. forsythia  | 2350824          |         | T. forsythia  | 101412 | 4%                       |
| 12      | P. gingivalis | 2047761          | 12      | P. gingivalis | 349551 | 17%                      |
|         | T. forsythia  | 2039390          |         | T. forsythia  | 290098 | 17%                      |
| Negative | P. gingivalis | 0               | Control | P. gingivalis | 0      | 0                        |
| Control | T. forsythia  | 0               | OUTSIDE | T. forsythia  | 0      | 0                        |
| Media   | PorG          | 3273565          | Inside  | PorG          | 599419 | 18%                      |
|         | TanF          | 3409120          |         | TanF          | 639808 | 19%                      |
tion. Moreover, the difference between outer and inner bacteria concentration was statistically significant at each time point.

Discussion

A tight integration between abutment and implant is one of the primary objectives of a TIPS during prosthesis phase and it is of paramount importance to reduce the risk of peri-implantitis (34, 35, 37, 51-90). This can happen also in patients with syndroms (91-93, 105-109) and tumors (94-98). Micro-cavities between implant and abutment favour bacterial leakage both from the external medium to the interior of the implant-abutment connection in a TPIS. The size of these micro cavities and gaps of a TPIS has been investigated by other Authors who tried to correlate its increase with bacterial leakage (49, 50, 99-103). The aim of this in vitro study was to evaluate the bacterial leakage along the implant-abutment connection by RT-PCR. The detection of implants external contamination evidences that micro cavities may be a passage to the external medium. In a recent in vitro study, do Nascimento et al. showed similar bacterial leakage through the interface implant-abutment of different TPISs. Bacterial leakage through the implant-abutment connection has also been shown in other in vitro studies (99).

In the present study demonstrated a low rate of movement of microorganisms from the implant internal region to the exterior, due to this TPIS type of connection, constructed to prevent leakage through any interface. Quirynen et al. detected higher bacterial leakage in the interior of implants, which were totally submersed in the culture medium. These Authors thus showed that bacterial leakage through the prosthetic screw also (100). Nakazato et al., however, established that it takes only 4 hours for bacterial colonies to form on abutment surfaces (101).

While conventional cultures detect only viable bacterial cells, RT-PCR studies compiles both viable and nonviable cells, and this may be a possible explanation for the differences detected by the two methods. Mombelli et al. described limitations in bacterial cell quantification in the conventional method observing a variation of up to 24% in the bacterial loading values in one single sample, as evidence of the limited precision of the method, especially when dealing with species with high aggregation tendencies (104, 110, 111). The limitation of this study may be the low number of microorganisms encountered in the implant interior, but new in vivo longitudinal studies are necessary to establish their influence in long-term clinical situations.

Conclusion

The RT-PCR has been shown to be more sensitive than the conventional bacterial culture method to detect in vitro contamination of dental implants. The detection of bacteria in the internal parts of this TPIS diminishes with time, suggesting reduction of bacterial viability and damage of genetic material. The RT-PCR may present advantages over the culture methods in the identification and quantification of bacteria associated with implant components and peri-implant tissues.

The reported results are similar to previous work (103). Konus Implant System® showed bacterial leakage similar respect others implant systems (18% Porphyromonas Gingivalis, 19% Tannerella Forsitya versus 20% of Bicon© and Ankylos© systems). In spite of the limits of our study, none TPIS has been demonstrated to perfectly close the gap between implant and abutment.

References

1. Rigo L, Viscioni A, Franco M, et al. Overdentures on implants placed in bone augmented with fresh frozen bone. Minerva Stomatol. 2011;60:5-14.
2. Carinci F, Brunelli G, Franco M, et al. A retrospective study on 287 implants installed in resorbed maxillae grafted with fresh frozen allogeneic bone. Clin Implant Dent Relat Res. 2010;12:91-98.

3. Visconti A, Rigo L, Franco M, et al. Reconstruction of severely atrophic jaws using homografts and simultaneous implant placement: a retrospective study. J Oral Implantol. 2010;36:131-139.

4. Franco M, Rigo L, Visconte A, et al. CaPO4 blasted implants inserted into iliac crest homologue frozen grafts. The Journal of oral implantology. 2009;35:176-180.

5. Visconti A, Franco M, Rigo L, et al. Implants inserted into homografts bearing fixed restorations. Int J Prosthodont. 2009;22:148-154.

6. Franco M, Visconti A, Rigo L, et al. Clinical outcome of narrow diameter implants inserted into allografts. J Appl Oral Sci. 2009;17:301-306.

7. Visconti A, Franco M, Rigo L, et al. Retrospective study of standard-diameter implants inserted into allografts. J Oral Maxillofac Surg. 2009;67:387-393.

8. Carinci F, Brunelli G, Zollino H, et al. Mandibles grafted with fresh-frozen bone: An evaluation of implant outcome. Implant Dentistry. 2009;18:86-95.

9. Carinci F, Brunelli G, Zollino I, et al. Mandibles grafted with fresh-frozen bone: an evaluation of implant outcome. Implant Dent. 2009;18:86-95.

10. Franco M, Tropina E, De Santis B, et al. A 2-year follow-up study on standard length implants inserted into alveolar bone sites augmented with homografts. Stomatologia. 2008;10:127-132.

11. Danza M, Paracchini L, Carinci F. Tridimensional finite element analysis to detect stress distribution in implants. Dental Cadmos. 2012;80:598-602.

12. Danza M, Grechi F, Zollino I, et al. Spiral implants bearing full-arch rehabilitation: Analysis of clinical outcome. Journal of Oral Implantology. 2011;37:447-455.

13. Danza M, Zollino I, Avantaggiato A, et al. Distance between implants has a potential impact of crestal bone resorption. Saudi Dental Journal. 2011;23:129-133.

14. Carinci F, Danza M. Clinical outcome of implants inserted in piezO split alveolar ridges: A pilot study. In: Perspectives on Clinical Dentistry. 2011;29-30.

15. Danza M, Zollino I, Guidi R, et al. Computer planned implantology: Analysis of a case series. In: ed. 4(eds. Perspectives on Clinical Dentistry. 2011;287-300.

16. Danza M, Carinci F. Flapless surgery and immediately loaded implants: a retrospective comparison between implantation with and without computer-assisted planned surgical stent. Stomatologia. 2010;12:35-41.

17. Danza M, Quaranta A, Carinci F, et al. Biomechanical evaluation of dental implants in D1 and D4 bone by Finite Element Analysis. Minerva stomatologica. 2010;59:305-313.

18. Danza M, Riccardo G, Carinci F. Bone platform switching: a retrospective study on the slope of reverse conical neck. Quintessence Int. 2010;41:35-40.

19. Danza M, Fromovich O, Guidi R, et al. The clinical outcomes of 234 spiral family implants. J Contemp Dent Pract. 2009;10:E049-056.

20. Calvo-Guirado JL, Ortiz-Ruiz AJ, Lopez-Mari L, et al. Immediate maxillary restoration of single-tooth implants using platform switching for crestal bone preservation: a 12-month study. Int J Oral Maxillofac Implants. 2009;24:275-281.

21. Danza M, Guidi R, Carinci F. Comparison between Implants Inserted Into Piezo Split and Unsplit Alveolar Crests. Journal of Oral and Maxillofacial Surgery. 2009;67:2460-2465.

22. Danza M, Scarano A, Zollino I, et al. Evaluation of biological width around implants inserted in native alveolar crest bone. Journal of Osseointegration. 2009;1:73-76.

23. Danza M, Zollino I, Guidi R, et al. A new device for impression transfer for non-parallel endosseous implants. Saudi Dental Journal. 2009;21:79-81.

24. Andreassi Bassi M, Lopez MA, Confalone L, et al. Clinical outcome of a two-piece implant system with an internal hexagonal connection: a prospective study. J Biolog Regul Homeost Agents. 2016;30:7-12.

25. Danza M, Guidi R, Carinci F. Spiral family implants inserted in postextraction bone sites. Implant Dent. 2009;18:270-278.

26. Lucchese A, Carinci F, Saggese V, et al. Immediate loading versus traditional approach in functional implantology. European Journal of Inflammation. 2012;10:55-58.

27. Traini T, Danza M, Zollino I, et al. Histomorphic-metric evaluation of an immediately loaded implant retrieved from human mandible after 2 years. International Journal of Immunopathology and Pharmacology. 2011;24:31-36.

28. Scarano A, Murmura G, Carinci F, et al. Immediately loaded narrow diameter dental implants: evaluation of retention, stability and comfort for the edentulous patient. European Journal of Inflammation. 2012;10:19-23.

29. Degidi M, Piattelli A, Carinci F. Clinical outcome of narrow diameter implants: a retrospective study of 510 implants. J Periodontol. 2008;79:49-54.

30. Degidi M, Piattelli A, Iezzi G, et al. Do longer implants improve clinical outcome in immediate loading? Int J Oral Maxillofac Surg. 2007;36:1172-1176.

31. Degidi M, Piattelli A, Carinci F. Immediate loaded dental implants: comparison between fixtures inserted in postextraction and healed bone sites. J Craniofac Surg. 2007;18:965-971.

32. Degidi M, Piattelli A, Iezzi G, et al. Retrospective study of 200 immediately loaded implants retaining 50 mandibular overdentures. Quintessence Int. 2007;38:281-288.

33. Degidi M, Piattelli A, Iezzi G, et al. Immediately loaded short implants: analysis of a case series of 133 implants. Quintessence Int. 2007;38:193-201.

34. Degidi M, Piattelli A, Iezzi G, et al. Wide-diameter im-
plants: Analysis of clinical outcome of 304 fixtures. Journal of Periodontology. 2007;78:52-58.
35. Degidi M, Piattelli A, Gehrke P, et al. Five-year outcome of 111 immediate nonfunctional single restorations. J Oral Implantol. 2006;32:277-285.
36. Degidi M, Piattelli A, Carinci F. Parallel screw cylinder implants: Comparative analysis between immediate loading and two-stage healing of 1005 dental implants with a 2-year follow up. Clinical Implant Dentistry and Related Research. 2006;8:151-160.
37. Degidi M, Piattelli A, Gehrke P, et al. Clinical outcome of 802 immediately loaded 2-stage submerged implants with a new grit-blasted and acid-etched surface: 12-month follow-up. Int J Oral Maxillofac Implants. 2006;21:763-768.
38. Degidi M, Piattelli A, Felice P, et al. Immediate functional loading of edentulous maxilla: a 5-year retrospective study of 388 titanium implants. J Periodontol. 2005;76:1016-1024.
39. Falisi G, Severino M, Rastelli C, et al. The effects of surgical preparation techniques and implant macrogeometry on primary stability: An in vitro study. Medicina Oral, Patologia Oral y Cirugia Bucal. 2017;22:e201-e206.
40. Pocaterra A, Caruso S, Bernardi S, et al. Effectiveness of platelet-rich plasma as an adjunctive material to bone graft: a systematic review and meta-analysis of randomized controlled clinical trials. International Journal of Oral and Maxillofacial Surgery. 2016;45:1027-1034.
41. Marrelli M, Pujia A, Palmieri F, et al. Innovative approach for the in vitro research on biomedical scaffolds designed and customized with CAD-CAM technology. International Journal of Immunopathology and Pharmacology. 2016;29:778-783.
42. Giuca MR, Pasini M, Giuca G, et al. Investigation of periodontal status in type 1 diabetic adolescents. European journal of paediatric dentistry : official journal of European Academy of Paediatric Dentistry. 2015;16:319-323.
43. Giuca MR, Pasini M, Caruso S, et al. Index of orthodontic treatment need in obese adolescents. International Journal of Dentistry. 2015;2015:
44. Caruso S, Sgolastra F, Gatto R. Dental pulp regeneration in paediatric dentistry: The role of stem cells. European Journal of Paediatric Dentistry. 2014;15:90-94.
45. De Vico G, Ottria L, Bollero P, et al. Aesthetic and functionality in fixed prostodontic: experimental and clinical analysis of the CAD-CAM systematic 3Shape. Oral Implantol (Rome). 2008;1:104-115.
46. Moretto D, Gargari M, Nordsjo E, et al. Immediate loading: a new implant technique with immediate loading and aesthetics: Nobel Active. Oral Implantol (Rome). 2008;1:50-55.
47. Spinelli D, De Vico G, Condò R, et al. Transcrestal guided sinus lift without grafting materials: A 36 months clinical prospective study. ORAL and Implantology. 2015;8:74-86.
48. Bartuli FN, Luciani F, Caddeo F, et al. Piezosurgery vs High Speed Rotary Handpiece: a comparison between the two techniques in the impacted third molar surgery. Oral Implantol (Rome). 2013;6:5-10.
49. Koka S, Razzoog ME, Bloem TJ, et al. Microbial colonization of dental implants in partially edentulous subjects. J Prosthet Dent. 1993;70:141-144.
50. Zipprich H, Miatke S, Hmaidouch R, et al. A New Experimental Design for Bacterial Microleakage Investigation at the Implant-Abutment Interface: An In Vitro Study. Int J Oral Maxillofac Implants. 2016;31:37-44.
51. Lauritano D, Martinelli M, Mucchi D, et al. Bacterial load of periodontal pathogens among Italian patients with chronic periodontitis: A comparative study of three different areas. Journal of Biological Regulators and Homeostatic Agents. 2016;30:149-154.
52. Lauritano D, Scapoli L, Mucchi D, et al. Infectogenomics: Lack of association between ivdr, ii6, iil0 polymorphisms and “red Complex” bacterial load in a group of Italian adults with chronic periodontal disease. Journal of Biological Regulators and Homeostatic Agents. 2016;30:155-160.
53. Checchi L, Gatto MR, Checchi V, et al. Bacteria prevalence in a large Italian population sample: A clinical and microbiological study. Journal of Biological Regulators and Homeostatic Agents. 2016;30:199-208.
54. Meynard F, Pasqualini ME, Rossi F, et al. Correlation between dysfunctional occlusion and periodontal bacterial profile. J Biol Regul Homeost Agents. 2016;30:115-121.
55. Lombardo L, Carinci F, Martini M, et al. Quantitative evaluation of dentin sialoprotein (DSP) using microbeads - A potential early marker of root resorption. ORAL and Implantology. 2016;9:132-142.
56. Lauritano D, Cura F, Candotto V, et al. Evaluation of the Efficacy of Titanium Dioxide with Monovalent Silver Ions Covalently Linked (Tiab) as an Adjuvant to Scaling and Root Planing in the Management of Chronic Periodontitis Using Pcr Analysis: A Microbiological Study. J Biol Regul Homeost Agents. 2015;29:127-130.
57. Scapoli L, Girardi A, Palmieri A, et al. Quantitative Analysis of Periodontal Pathogens in Periodontitis and Gingivitis. J Biol Regul Homeost Agents. 2015;29:101-110.
58. Lauritano D, Cura F, Candotto V, et al. Periodontal Pockets as a Reservoir of Helicobacter Pylori Causing Relapse of Gastric Ulcer: A Review of the Literature. J Biol Regul Homeost Agents. 2015;29:123-126.
59. Scapoli L, Girardi A, Palmieri A, et al. Interleukin-6 Gene Polymorphism Modulates the Risk of Periodontal Diseases. J Biol Regul Homeost Agents. 2015;29:111-116.
60. Carinci F, Girardi A, Palmieri A, et al. LAB®-Test 1: Peri-Implantitis and bacteriological analysis. European Journal of Inflammation. 2012;10:91-93.
61. Carinci F, Girardi A, Palmieri A, et al. LAB®-test 2: Microflora and periodontal disease. European Journal of Inflammation. 2012;10:95-98.
62. Carinci F, Girardi A, Palmieri A, et al. Lab®-test 3: Genetic susceptibility in periodontal disease. European Journal of Inflammation. 2012;10:99-101.
63. Scapoli L, Girardi A, Palmieri A, et al. IL6 and IL10 are genetic susceptibility factors of periodontal disease. Dent Res J (Isfahan). 2012;9:S197-201.
64. Carinci F, Girardi A, Palmieri A, et al. Lab-test 2: microflora and periodontal disease. European Journal of Inflammation. 2012;10:95-98.
65. Cura F, Palmieri A, Girardi A, et al. Lab-Test((R)) 4: Dental caries and bacteriological analysis. Dent Res J (Isfahan). 2012;9:S139-141.
66. Roncati M, Lauritano D, Cura F, et al. Evaluation of light-emitting diode (led-835 nm) application over human gingival fibroblast: An in vitro study. Journal of Biological Regulators and Homeostatic Agents. 2016;30:161-167.
67. Caccianiga G, Rey G, Piausco A, et al. Oxygen high level laser therapy is efficient in treatment of chronic periodontitis: A clinical and microbiological study using PCR analysis. Journal of Biological Regulators and Homeostatic Agents. 2016;30:87-97.
68. Lauritano D, Bignozzi CA, Pazzi D, et al. Evaluation of the efficacy of a new oral gel as an adjunct to home oral hygiene in the management of chronic periodontitis. A microbiological study using PCR analysis. J Biol Regul Homeost Agents. 2016;30:123-128.
69. Carinci F, Palmieri A, Girardi A, et al. Aquolab® ozone-therapy is an efficient adjuvant in the treatment of chronic periodontitis: A case-control study. Journal of Orofacial Sciences. 2015;7:27-32.
70. Lauritano D, Cura F, Gaudio RM, et al. Polymerase Chain Reaction to Evaluate the Efficacy of Silica Dioxide Colloidal Solutions in the Treatment of Chronic Periodontitis: A Case Control Study. J Biol Regul Homeost Agents. 2015;29:131-135.
71. Lauritano D, Petruzzi M, Nardi GM, et al. Single Application of a Desiccating Agent in the Treatment of Recurrent Aphthous Stomatitis. J Biol Regul Homeost Agents. 2015;29:59-66.
72. Carinci F, Lauritano D, Cura F, et al. Prevention of bacterial leakage at implant-Abutment connection level: An in vitro study of the efficacy of three different implant systems. Journal of Biological Regulators and Homeostatic Agents. 2016;30:69-73.
73. El Haddad E, Gianni AB, Mancini GE, et al. Implant-abutment leaking of replace conical connection nobel biocare® implant system. An in vitro study of the microbiological penetration from external environment to implant-abutment space. ORAL and Implantology. 2016;9:76-82.
74. Mancini GE, Gianni AB, Cura F, et al. Efficacy of a new implant-abutment connection to minimize microbial contamination: An in vitro study. ORAL and Implantology. 2016;9:99-105.
75. Roncati M, Lueches A, Carinci F. Non-Surgical treatment of peri-Implantitis with the adjunctive use of an 810-nm diode laser. Journal of Indian Society of Periodontology. 2013;17:812-815.
76. Scaranò A, Tripodi D, Carinci F, et al. Biofilm formation on titanium alloy and anatase-Bactercline® coated titanium healing screws: An in vivo human study. Journal of Osseointegration. 2013;5:8-12.
77. Brunelli G, Carinci F, Zollino I, et al. Sem evaluation of 10 infected implants retrieved from man. European Journal of Inflammation. 2012;10:7-12.
78. Scaranò A, Sinjari B, Di Orio D, et al. Surface analysis of failed oral titanium implants after irradiated with ErCr:ysgg 2780 laser. European Journal of Inflammation. 2012;10:49-54.
79. Brunelli G, Carinci F, Zollino I, et al. Peri-implantitis. A case report and literature review. European Journal of Inflammation. 2012;10:1-5.
80. Scaranò A, Piattelli A, Polimeni A, et al. Bacterial adhesion on commercially pure titanium and anatase-coated titanium healing screws: An in vivo human study. Journal of Periodontology. 2010;81:1466-1471.
81. Grecchi F, Zollino I, Candotto V, et al. A case of mandible osteonecrosis after a severe perimplant infection. Dent Res J (Isfahan). 2012;9:S233-236.
82. Carinci F, Farina A, Zanetti U, et al. Alveolar ridge augmentation: a comparative longitudinal study between calvaria and iliac crest bone grafts. J Oral Implantol. 2005;31:39-45.
83. Carinci F, Pezzetti F, Volinia S, et al. Analysis of MG63 osteoblastic-cell response to a new nanoporous implant surface by means of a microarray technology. Clinical Oral Implants Research. 2004;15:180-186.
84. Oliveira DP, Palmieri A, Carinci F, et al. Osteoblasts behavior on chemically treated commercially pure titanium surfaces. J Biomed Mater Res A. 2014;102:1816-1822.
85. Andreasi Bassi M, Lopez MA, Confalone L, et al. Hydraulic sinus lift technique in future site development: clinical and histomorphometric analysis of human biopsies. Implant Dent. 2015;24:117-124.
86. El Haddad E, Lauritano D, Carinci F. Interradicular septum as guide for pilot drill in postextractive implantology: a technical note. J Contemp Dent Pract. 2015;16:81-84.
87. Gargari M, Comuzzi L, Bazzato MF, et al. Treatment of peri-implantitis: Description of a technique of surgical 2 detoxification of the implant. A prospective clinical case series with 3-year follow-up. ORAL and Implantology. 2015;8:1-11.
88. Azzi L, Carinci F, Gabaglio S, et al. Helicobacter pylori in periodontal pockets and saliva: A possible role in gastric infection relapses. Journal of Biological Regulators and Homeostatic Agents. 2017;31:257-262.
89. Tettamanti L, Gaudio RM, Cura F, et al. Prevalence of periodontal pathogens among Italian patients with...
chronic periodontitis: A retrospective study on 2992 patients. ORAL and Implantology. 2017;10:28-36.
90. Tettamanti L, Gaudio RM, Iapichino A, et al. Genetic susceptibility and periodontal disease: A retrospective study on a large italian sample. ORAL and Implantology. 2017;10:20-27.
91. Carinci F, Avantaggiato A, Curioni C. Crouzon syndrome: Cephalometric analysis and evaluation of pathogenesis. Cleft Palate-Craniofacial Journal. 1994;31:201-209.
92. Bodo M, Carinci F, Baroni T, et al. Apert’s syndrome: Differential in vitro production of matrix macromolecules and its regulation by interleukins. European Journal of Clinical Investigation. 1997;27:36-42.
93. Martinelli M, Scapoli L, Palmieri A, et al. Study of four genes belonging to the folate pathway: transcobalamin 2 is involved in the onset of non-syndromic cleft lip with or without cleft palate. Human mutation. 2006;27:294.
94. Carinci F, Stabellini G, Calvitti M, et al. CD44 as prognostic factor in oral and oropharyngeal squamous cell carcinoma. J Craniomax. Surg. 2002;13:85-89.
95. Mariani G, Calastrini C, Carinci F, et al. Ultrastructural features of cyclosporine A-induced gingival hyperplasia. Journal of Periodontology. 1993;64:1092-1097.
96. Francioso F, Carinci F, Tosi L, et al. Identification of differentially expressed genes in human salivary gland tumors by DNA microarrays. Molecular Cancer Therapeutics. 2002;1:533-538.
97. Bodo M, Lilli C, Bellucci C, et al. Basic fibroblast growth factor autocrine loop controls human osteosarcoma phenotyping and differentiation. Molecular Medicine. 2002;8:393-404.
98. Carinci F, Lo Muzio L, Piattelli A, et al. Potential markers of tongue tumor progression selected by cDNA microarray. International Journal of Immunopathology and Pharmacology. 2005;18:513-524.
99. do Nascimento C, Barbosa RE, Issa JP, et al. Bacterial leakage along the implant-abutment interface of premaxilled or cast components. Int J Oral Maxillofac Surg. 2008;37:177-180.
100. Quirynen M, Alsadi G, Pauwels M, et al. Microbiological and clinical outcomes and patient satisfaction for two treatment options in the edentulous lower jaw after 10 years of function. Clin Oral Implants Res. 2005;16:277-287.
101. Nakazato G, Tsuchiya H, Sato M, et al. In vivo plaque formation on implant materials. Int J Oral Maxillofac Implants. 1989;4:321-326.
102. Momberli A, Buser D, Lang NP. Colonization of osseointegrated titanium implants in edentulous patients. Early results. Oral Microbiol Immunol. 1988;3:113-120.
103. Alolse JP, Curcio R, Laporta MZ, et al. Microbial leakage through the implant-abutment interface of Morse taper implants in vitro. Clin Oral Implants Res. 2010;21:328-335.
104. Leonhardt A, Adolfsson B, Lekholm U, et al. A longitudinal microbiological study on osseointegrated titanium implants in partially edentulous patients. Clin Oral Implants Res. 1993;4:113-120.
105. Lauritano D, Avantaggiato A, Candotto V, et al. Effect of somatostatin on dental pulp stem cells. Journal of biological regulators and homeostatic agents. 2015;29(3 Suppl 1):48-58.
106. Grechi F, Perale G, Candotto V, et al. Reconstruction of the zygomatic bone with smartbone®: case report. Journal of biological regulators and homeostatic agents. 2015;29(3 Suppl 1):42-47.
107. Lauritano D, Avantaggiato A, Candotto V, et al. Insulin activity on dental pulp stem cell differentiation: an in vitro study. Journal of biological regulators and homeostatic agents. 2015;29(3 Suppl 1):48-58.
108. Baj A, Trapella G, Lauritano D, et al. An overview on bone reconstruction of atrophic maxilla: success parameters and critical issues. Journal of biological regulators and homeostatic agents. 2016;30(2 Suppl 1):209-215.
109. Tettamanti L, Bassi MA, Trapella G, et al. Applications of biomaterials for bone augmentation of jaws: clinical outcomes and in vitro studies. Oral Implantol (Rome). 2017 Apr 10;10(1):37-44. eCollection 2017 Jan-Mar.
110. Baj A, Lo Muzio L, Lauritano D, et al. Success of intermediate versus standard loaded implants: a short literature review. Journal of biological regulators and homeostatic agents. 2016;30(2 Suppl 1):183-188.
111. Baj A, Sollazzo V, Lauritano D, et al. Lights and shadows of bone augmentation in severe resorbed mandible in combination with implant dentistry. Journal of biological regulators and homeostatic agents. 2016;30(2 Suppl 1):177-182.

Correspondence to:
Lucia Tettamanti
Department of Medicine and Surgery
University of Insubria
Via Piatti 10
21100 Varese, Italy
Phone: +39.0332-825625 - Fax: +39.0332-825655
E-mail: lucia.tettamanti@uninsubria.it