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PERI-IMPLANT BIOLOGICAL COMPLICATIONS AND OVERDENTURES

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ABSTRACT

The main objective of this work was to study the phenomena associated with implant failure and peri-implant diseases, in oral rehabilitations with overdentures. Patients were evaluated and a sample from peri-implant crevicular fluid (PICF) was collected for detection of interleukin-1 (*IL1*) polymorphisms and identification of periodonto-pathogenic bacteria by PCR. A better understanding of implant failure mechanisms and the knowledge of microbial composition of peri-implant sulcus is clinically essential to prevent complications which can compromise the success of oral rehabilitations with osseointegrated implants.

Keywords: implant failure, peri-implant disease, *IL1* polymorphisms, overdentures

INTRODUCTION

An implant-supported or implant-retained overdenture consists in a removable dental prosthesis that covers and rests on one or more dental implants (The glossary of prosthodontics terms, 2005) and is retained by an attachment system. This is a very satisfactory prosthodontic option for patients and dentists since implants are used successfully as abutments on total and partially edentulous patients. It is even more fitting in cases of prosthetic instability and atrophic jaws (Assunção, 2007). However, sometimes implant loss and complications (biological and technical) may occur. Pathological conditions may develop in the peri-implant tissues putting implants and oral rehabilitations at risk and potentially affecting patient's health (Berglundh, 2002; Pjetursson, 2004).

Lang and colleagues (Lang, 2004) described the following terms related to biologic complications/peri-implant disease: mucositis, peri-implantitis, and soft tissue complications (fistula, excessive swelling, hyperplasia, redness, among others). Peri-implant diseases may only affect the peri-implant mucosa (peri-implant mucositis) or also involve the supporting bone (peri-implantitis) (Zitzmann, 2008).

Pathogenic bacteria and other environmental factors have been reported to be involved in the pathogenesis of peri-implant diseases (Heitz-Mayfield, 2008). In this review, poor oral hygiene, history of periodontitis and smoking habit were described as risk factors for peri-implant disease. Regarding diabetes and alcohol consumption, scientific evidence is still limited. Furthermore, the interleukin 1 (*IL1*) genotype composition and implant surface are considered controversial risk indicators for peri-implant disease. It has been reported a synergistic effect between a positive *IL1* genotype and smoking, that puts implants at higher risk of developing biologic complications (Feloutzis, 2003; Gruica, 2004; Jansson, 2005).

The most important factor that leads to peri-implantitis with bone loss seems to be the inflammatory process, due to accumulation of infectious plaque (Albrektsson, 1994). It is

believed that the clinical course of the disease may be dependent mainly on the host response to bacterial toxins (Page, 1997). The lipopolysaccharide (LPS) of bacterial wall stimulates the release of IL1 and tumor necrosis factor – alfa (TNF-α) by monocytes and macrophages (Santamaria, 1989). These proinflammatory mediators will in turn stimulate the production of prostaglandins (particularly PGE2) and matrix metalloproteinases (MMP) associated to bone resorption and destruction of connective tissue, respectively (Gruica, 2004).

Interleukin 1A (IL1A), interleukin 1B (IL1B) and their natural specific inhibitor interleukin 1 receptor antagonist (IL1RN) play a key role in the regulation of the inflammatory response. Genes which modulate the host response can influence the severity of periodontitis (Woo, 2000), and some genetic polymorphisms of *IL1* have been associated with the occurrence and progression of pathological clinical situations in oral rehabilitation using dental implants (Vaz, 2012; Lachmann, 2007; Montes 2009; Dirschnabel, 2011; Jansson, 2005).

The genetic polymorphisms more studied in the susceptibility to peri-implant disease or in failure of oral rehabilitation with dental implants are at the positions -889 of the *IL1A* gene and +3953 of the *IL1B* gene (Andreiotelli, 2008). The *IL1RN* gene polymorphism at position +2018 has been studied in the development of arthritis (Laine, 2006).

In a Portuguese population rehabilitated with dental implants, the prevalence of polymorphisms of *IL1A* and *IL1B* genes (positions -889 and +3953) was 33.5% (Vaz, 2009), value similar to that described in other European Caucasian populations (Kornmann, 1997; Lang, 2000).

The microflora present in the peri-implant sulcus of patients with peri-implantitis is very similar to that existing in the gingival sulcus of patients with chronic periodontitis (Berglundh, 2011). The microbiota associated with peri-implant disease is mixed, varied and, in many cases, dominated by Gram-negative anaerobic bacteria (Mombelli, 2011). Some studies reported high prevalence of periodontal pathogenic microorganisms including species from the red complex (*Porphyromonas gingivalis - Pg*, *Tannerella forsythia - Tf*, *Treponema denticola - Td*) and from the orange complex (*Prevotella intermedia - Pi*, e *Fusobacterium sp.) Aggregatibacter actinomycetemcomitans (Aa)* was also detected at peri-implantitis sites (Heitz-Mayfield, 2010). Lee *et al*. (Lee, 1999) concluded that a history of periodontitis had a greater impact on the peri-implant microbiota than implant loading time; however, the major influence on the peri-implant microbiota was the microbiota on remaining teeth.

The beneficial effects of chemical and mechanical interventions to alter the biofilm show that microorganisms are involved in pathological process but do not prove that these are always the origin of this condition (Mombelli, 2011). Little is known about the influence of *IL-1* genotype in the composition of peri-implant microflora.

To better understand the influence of the different genotype combinations for *IL1* gene in peri-implant biofilm, it is essential to study the occurrence of peri-implant inflammatory disease, their extent and severity, using the individual like unit of study.

OBJECTIVES

The aims of this study were to examine the relation between the allelic variants of the *IL-1* gene complex polymorphisms and failure of osseointegrated dental implants supporting overdentures and to describe the microbiota associated with different biologic complications.

MATERIAL AND METHODS

This investigation was undertaken at the Faculty of Dental Medicine, University of Porto, Portugal. The Ethics Committee approved the study, and all patients gave written informed consent before the study started.

Sixteen patients, treated with nineteen implant-assisted overdentures (inclusion criteria) at the clinical faculty or in a private practice, were called for an appointment. Implants with less than 1 year in function (time between the prosthesis installation and the clinical examination) were excluded from the study. During the visit, medical and dental history was assessed using a structured questionnaire.

Subject characteristics collected were gender, age, partial or total edentulism, diabetes, history of periodontitis, past and present smoking habits, alcohol consumption, past and present medication. Implant characteristics collected for screening were localization (maxillary/mandibular), distribution in dentate and edentulous patients, and duration in function. Implant-supported overdentures were classified according to localization and retention system.

Clinical and Radiographic procedures

Systematic monitoring of peri-implant tissues is recommended for the diagnosis of peri-implant disease. After the collection of peri-implant crevicular fluid, the clinical measurements were made in all implants supporting the overdenture.

The diagnostic parameters included modified plaque index (mPlI) (Mombelli, 1987), modified bleeding index (mBlI) (Mombelli, 1987), probing depth (PD) at four sites around each selected implant (mesial, buccal, distal, palatal/lingual) and other potential signs of inflammation (suppuration, hyperplasia, fistula, mobility, redness and pain). The depth of the peri-implant pocket was measured with a Williams probe (Hu-Friedy®, USA). From a clinical point of view, absence of bleeding on probing (BOP) around implants and PS less than 3 mm would indicate healthy peri-implant tissues (Lang, 2000). The periodontal status of partial edentulous patients was evaluated by teeth mobility and radiographic bone level of the remaining teeth. The peri-implant bone loss was evaluated on panoramic radiography, performed for less than 6 months or before the clinical examination.

From the clinical data available, the time since the prosthesis installation and the presence of biological complications at the examination were used for the analysis. Each patient was classified as healthy or with complication, which refers to the presence or absence of any type of implant biological complication. At the moment of the examination, a total of 63 implants were clinically examined and classified in classes considering the condition of peri-implant tissues: healthy, mucositis, peri-implantitis, and other biological complications.

Determination of *IL1* genotype and microbiological procedures

The peri-implant crevicular fluid (PICF) was collected before peri-implant probing. If present, supragingival plaque deposits were carefully removed with a cotton pellet. The peri-implant sulcus was sampled by inserting one sterile paper point #30 (Dentsply De Trey®, USA) at each of the following four locations: mesial, buccal, distal, and palatal/lingual. After 10 seconds, the paper points from the four implant sites was withdrawn and pooled in an eppendorf tube. The samples were obtained from one implant in each patient.

The biologic material from peri-implant sulcus was analyzed for detection of *IL1* polymorphisms and for identification of periodonto-pathogenic bacteria by polymerase chain reaction (PCR).

The DNA was extracted from the cells presented in the PICF. The result reported the presence of allele '1' or '2'. A homozygous type was considered if there was an allele 2 at both positions (-889, +3953) of the *IL1A* and *IL1B* genes. A heterozygous type was considered if there was only one allele 2 at both positions. The *IL1* genotype was considered positive only if the allele 2 was present at both positions of the two studied genes *(IL1A, IL1B*). So, if there was no allele 2 or if there was an allele 2 only at one position of the two studied genes (*IL1A* or *IL1B*), the *IL1* genotype were considered negative. Nevertheless our analysis was not limited to the *IL1* combined genotype. We did the analysis of allelic composition because if we consider only the genotype, the heterozygous subjects were underestimated.
Each sample was also used for the detection of the following four species of periodontopathic bacteria: *Porphyromonas gingivalis (P.g.), Bacteroides forsythus (B.f.), Fusobacterium nucleatum (F.n.),* and *Actinomyces actinomycetemcomitans (A.a).*

Data analysis/Statistical analysis

The collected data were analyzed in the software SPSS 20.0® and according to the nature of the variables in study. The statistical analysis was descriptive because of the reduced sample size at that time.

RESULTS

All patients (n=16) were Caucasian (12 female and 4 male). The mean age was 71.5 years (range 58 to 82 years). There were 10 patients (62.5%) with partial edentulism and 6 (37.5%) with total edentulism. All patients were non-smokers. Concerning history of periodontitis, 9 patients (56%) referred mobility or periodontal disease like a reason for their tooth loss. At examination, 18.75% of patients were considered healthy and 81.25% presented at least one biological complication. Only one patient presented an *IL1* genotype positive (6.25%). The distribution of variables related to the patients is shown in Table 1.

In a retrospective view, implant loss occurred to three subjects: two early implant loss involving 3 implants; and one late implant loss involving 2 implants. None of these cases presented a positive *IL1* genotype.

The total number of implants examined was 63. Thirty two were located at the maxilla and the others thirty three at the mandible. At clinical examination, the implants were classified concerning diagnostic parameters and inflammation signs. So, 27% were considered healthy, 53.4% presented mucositis and 20.6% presented peri-implantitis. Hyperplasia was other biologic complication very frequent (30.2%) that occurred merely in cases with bar attachment systems. The distribution of variables related to the implants is shown in Table 2.

All examined implants supported 19 removable prostheses. The overdentures were divided according to the retention system and the localization (Table 3). The number of implants supporting an overdenture varied from 1 to 4. However, 3 patients presented two overdentures (an upper and a lower prosthesis) and, in each of them, 8 implants were analyzed. The time since the prosthetic reconstruction varied between 1 year and 5 months and 12 years and 5 months (mean time 5.5 years).

Table 1 - Distribution of different variables: patients

Patient variables	**N**	**%**
Overall	**16**	100
Male	4	25.00
Female	12	75.00
Partial edentulous	10	62.50
Total edentulous	6	37.50
History of periodontitis	9	56.25
Smokers	0	0.00
Non smokers	16	100
Diabetes	1	6.25
Bisphosphonates	1	6.25
Healthy patients	3	18.75
With biologic complication	13	81.25
IL1 genotype positive	1	6.25
IL1 genotype negative	15	93.75
Allele 1 IL1A homozygoty, Allele 1 IL1B homozygoty	8	50.00
Allele 1 IL1A homozygoty, Allele 2 IL1B heterozygoty	2	12.50
Allele 2 IL1A heterozygoty, Allele 1 IL1B homozygoty	2	12.50
Allele 2 IL1A heterozygoty, Allele 2 IL1B heterozygoty	3	18.75
Allele 2 IL1A homozygoty , Allele 2 IL1B homozygoty	1	6.25

Table 2 - Distribution of different variables: implants

Implant variables	**N**	**%**
Overall	**63**	100
Localization		
Maxilla	32	50.8
Mandible	31	49.2
Patients		
Dentate	36	57.1
Edentulous	27	42.9
Overdenture		
Bar	52	82.5
Ball	10	15.9
Locator	1	1.6
Clinical examination		
Healthy	17	27.0
Peri-mucositis	33	52.4
Peri-implantitis	13	20.6
Hyperplasia	21	33.3
Redness	11	17.5
Suppuration	2	3.2
Pain/Mobility	2	3.2

Table 3 - Distribution of implant-supported overdentures (n=19)

Overdenture	Maxillae	Mandibular	Total
Bar	8	6	**14**
Ball	0	4	**4**
Locator	1	0	**1**
Total	**9**	**10**	**19**

Only *B. forsythus* was identified in the PICF of an implant with light bleeding. This case was a negative *IL1* genotype. None of the others species of bacteria (*P.g.*, *F.n.* and *A.a.*) were detected by PCR.

DISCUSSION AND CONCLUSIONS

In the present study, all patients wore at least one implant-supported overdenture and the mean time in function was 5.5 years. All implants were analyzed for implant failure and biological complications in relation to their *IL1* genotype status. Only one subject was considered positive *IL1* genotype. However, if we consider the allelic combination, the three heterogynous types could be in higher risk for biological complications. The proportion of positive *IL1* genotype (6.25%) is lower and is not in agreement with a previous report of a Caucasian Portuguese population (Vaz, 2009), possibly due to the reduced sample size.

Few studies provided data on the prevalence of peri-implant diseases. A review article (Zitzmann, 2008) concluded that: peri-implant mucositis occurred in 80% of the subjects and in 50% of the implant sites; peri-implantitis was identified in 28% and >56% of subjects and in 12% and 43% of implant sites. In the present study, 80% of patients presented some biological complication at the moment of examination. At implant level, the percentages of healthy implants, peri-mucositis and peri-implantitis were 27%, 52.4% and 20.6% respectively.

A systematic review, that addressed the incidence of implant loss and complications of oral implants (Berglundh, 2002), reported 2.5% implant loss prior to the placement of overdentures and nearly 6% implant loss during 5 years of function. In this study, it is also stated that the soft tissue complications (pain, hyperplasia, suppuration and fistula), as well as technical complications (implant components and suprastructures), have a higher incidence in cases of overdentures compared with fixed restorations. Regarding the occurrence of peri-implantitis, that is to say a bone loss greater than 2.5 mm, the information is limited (Berglundh, 2002).

There is little scientific information about the occurrence of implant biological complications particularly in implant-supported overdentures, and much less about the influence of *IL1* allelic combinations on the development of inflammatory lesions on those peri-implant tissues.

When *B. forsythus* was identified, it seems that this bacteria was probably more implicated with the peri-implant condition, rather than the host response. In the other ones, it seems that the host response has more influence than the bacteria. When no bacteria were identified, we can presume that they were not present, at least on the tested implants, or the crevicular fluid collected was not sufficient to the analysis. However, we should also consider that other

periodonthopathic species, not tested in the present study, could have been present and contributing to the clinical situation.

The sample and the collected data were insufficient to conclude any association between the *IL1* genetic polymorphisms and the occurrence of peri-implant disease.

A better understanding of implant failure mechanisms and the knowledge of microbial composition of peri-implant sulcus is clinically essential to prevent complications which can compromise the success of oral rehabilitations with osseointegrated implants. A more extensive sample is needed to understand the challenge between the host response and the peri-implant bacteria in the pathogenesis of peri-implant diseases.

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