Revista Portuguesa de Estomatologia, Medicina Dentária e Cirurgia Maxilofacial

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Original research

IL1RN gene polymorphism in a Portuguese population with implant-supported overdentures – An observational study

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ARTICLE INFO

Article history:
Received 15 July 2015
Accepted 23 September 2015
Available online 5 December 2015

Keywords:
Dental implants
Genetic polymorphisms
Interleukin 1
IL1RN

ABSTRACT

Objectives: This study aimed to evaluate the frequency of the different alleles of the VNTR *IL1RN* gene (86 bp RP, intron 2), in a Portuguese Caucasian population with implant-supported overdentures.

Methods: Fifty-eight Caucasians rehabilitated with implant overdentures for at least 6 months, were randomly recruited from the Removable Prostheses Forms used in Faculty of Dental Medicine, University of Porto. After clinical examination, DNA was obtained through oral mucosa swab. PCR was used to identify the *IL1RN* gene alleles. The frequency estimates and the corresponding 95% CI for alleles and genotypes of the *IL1RN* gene were calculated using the exact binomial test.

Results: The population included 44 females and 14 males. Only 2 subjects were smokers; 6 subjects had diabetes and 5 had chronic gastritis. The most frequent allele of *IL1RN* gene was allele 5, with an estimated frequency of 58.6%, followed by the allele 4 with a frequency of 48.3%. The alleles 1 and 2 were not detected. The most frequent genotype was allele 5/allele 5, followed by the allele 4/allele 4.

Conclusions: Allele 5 was the most frequent *IL1RN* allele and allele 5/allele 5 was the most frequent genotype. Further studies are required in order to understand the role of alleles 5 and 4, as well as of the allelic combinations of the *IL1RN* gene polymorphism, on the development of biological complications with dental implants.

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http://dx.doi.org/10.1016/j.rpemd.2015.09.003

Polimorfismos do gene *IL1RN* numa população Portuguesa com sobredentaduras implanto-suportadas – um estudo observacional

Palavras-chave:
Implantes dentários
Polimorfismos genéticos
Interleucina 1
IL1RN

RESUMO

Objetivos: Este estudo teve como objetivo avaliar a frequência dos diferentes alelos do gene *IL1RN* VNTR (86 bp, intrão 2), numa população Caucasiana Portuguesa com sobredentaduras implanto-suportadas.

Métodos: Cinquenta-e-oito caucasianos reabilitados com sobredentaduras implantares por pelo menos 6 meses, foram recrutados aleatoriamente dos formulários de Prótese Removível da Faculdade de Medicina Dentária da Universidade do Porto. Após exame clínico, o ADN foi obtido por esfregaço da mucosa oral. A técnica PCR foi utilizada para identificar os alelos do gene *IL1RN*. A estimativa da frequência e respetivos IC a 95% dos alelos e genótipos *IL1RN* foram calculados usando o teste binomial exato.

Resultados: A população incluiu 44 mulheres e 14 homens. Apenas e indivíduos eram fumadores; 6 indivíduos apresentavam diabetes e 5 apresentavam gasrite crónica. O alelo 5 foi o alelo mais frequente do gene *IL1RN*, com uma frequência estimada de 58,6%, seguido do alelo 4 com uma frequência de 48,3%. Os alelos 1 e 2 não foram detetados. O genótipo mais frequente foi alelo 5/alelo 5, seguido de alelo 4/alelo 4.

Conclusões: O alelo 5 foi o alelo mais frequente do gene *IL1RN* e alelo 5/alelo 5 foi o genótipo mais frequente. São necessários mais estudos para se compreender o papel dos alelos 5 e 4, bem como das combinações de alelos do polimorfismo do gene *IL1RN*, no desenvolvimento de complicações biológicas com implantes dentários.

Introduction

Oral rehabilitation with dental implants has become increasingly relevant, given the evolution and diversity of the existing implant systems and their accessibility to the population. In general, dental implant rehabilitation can provide predictable and lasting results in the replacement of missing teeth and preservation of the adjacent natural tooth structures.[1–5]

Oral implants have become a widespread practice and their popularity will probably increase in the next few years.[6] Consequently, cases of peri-implant complications and implant failure tend to increase.[7] The clinical observation of repetitive unsuccessful dental implants in certain individuals has raised some questions related to host susceptibility to dental implant failure.[8] Several risk factors for implant failure were pointed out: hypertension, cardiovascular diseases, diabetes, autoimmune disorders, osteoporosis, bisphosphonate therapy, radiotherapy, history of periodontitis, smoking, implant site bone quality and genetic traits.[9] In fact, in a specific group of individuals, some specific host characteristics, which may disturb the osseointegration process, were suggested to be influenced by genetic factors.[8,10,11] Moreover, the number, identity and role of regulatory factors that can determine and maintain the success of osseointegration process are still a mystery.[9]

Nowadays, genetics research is concerned with studying DNA sequence variations (polymorphisms) and potentially associating them with increased risks for developing a particular condition or disease by a restricted population. In fact, these DNA variations may condition the gene transcription rate, the messenger RNA stability, or even the amount and activity of the produced protein.[12]

In the last years, several studies have pointed out the impact of certain interleukin-1 (IL1) gene single nucleotide polymorphisms (SNP) in the host response and in the development of peri-implant biological complications.[6,8,13–21]

More recently, some authors have suggested the existence of a possible relationship between an 86 bp (base pairs) repeat polymorphism (a variable number tandem repeat, VNTR) in intron 2 of the interleukin-1 receptor antagonist gene (*IL1RN*) and the development of biological implant complications, such as implant loss and peri-implantitis.[11,22,23]

Interleukin-1 (IL1) is a potent proinflammatory mediator mainly released by monocytes, macrophages, and dendritic cells, against microbial pathogens. This action is induced by lipopolysaccharides from gram-negative bacteria, present in the peri-implant sulcus. The interleukin-1 protein has two distinct structural forms encoded in two different genes – alpha in *IL1A* and beta in *IL1B* – located in the same chromosome 2 (2q13–q21).[24]

The interleukin-1 receptor antagonist (IL1RN) is a cytokine that binds to IL1 receptors, inhibiting their connection with IL1A and IL1B. Thus, the IL1RN molecule competes with IL1A and IL1B in target cells and acts as a negative regulator, with an anti-inflammatory effect. The *IL1RN* gene is also located in chromosome 2 (2q14.2).[25]

The reported VNTR of the *IL1RN* gene (intron 2) includes a variation of 2–6 repeats (RP), which results in 5 different alleles: 4 RP for allele 1, 2 RP for allele 2, 3 RP for allele 3, 5 RP for allele 4 and 6 RP for allele 5. Allele 1 was reported as the most common of these alleles, followed by allele 2. The remaining alleles