Perspective

Genetic Risk Assessment of Periodontal Disease during Dental Treatments

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Abstract

Periodontal diseases (PD) are extremely prevalent worldwide, affecting roughly half of the adult population. Any person who has a known susceptibility to periodontal disease and needs prosthetic or implant-prosthetic therapy (PIT) is recommended to undergo genetic testing to see if he/she is genetically predisposed to the development of periodontal disease, because such a patient is at increased risk of developing PD during or after the dental treatment. In other words, it seems beneficial to use a genetic test for identifying those most at risk of PD and to subject them to oral hygiene protocols. Several studies have investigated the association between some markers [such as interleukin (IL)-1, 4, 6, 10] polymorphisms and periodontitis susceptibility but with conflicting results. We recently reported that polymorphisms of IL6 and IL10 constitute risk factors for chronic periodontitis; therefore, genetic tests for these two factors are promising for constructing efficient preventive protocols during or after PIT.

INTRODUCTION

Molecular tests based to association studies between genetic markers and periodontal disease (PD) are potentially useful to detect high risk patients which have no clinical signs, since PD clinically arises in middle age. Since PD is a multifactorial disease (based both on genetic and environmental factors), differences in host response to oral micro flora load may be explained by different genetic background. New knowledge’s would highlight causes, pathogenesis, and onset of different PD and best treatment protocols to be applied. In addition, new researches about genetic risk factors would help to develop new diagnostic tools for prevention and/or early treatment of PD. Periodontal disease

PD is extremely prevalent worldwide, affecting roughly half of the adult population. PD is a multifactorial disease in which both environmental and genetic factors play a role, and its progression is related to periodontal pockets micro biota where both the amount and the presence of specific pathogen bacterial species represents risk factors. Additional risk factors are smoking and diabetes. However, a range of host genetic factors can influence individual susceptibility to PD and are able to influence the clinical aspects and rate of progression of the disease [1].

Genetic risk of PD

The discovery that genetics influences the development of PD goes back about 30 years ago. This new evidences has shown that PD, like other diseases (diabetes, cancer, etc.), requires a genetic predisposition to develop [2,3].

Individuals respond differently to the attack of the oral microflora according to their genetic predisposition. Also genetics determines how each person interacts with environmental factors (such as the oral biofilm) in the onset of PD. The relationship between genetic and environmental factors determines the onset of PD. Lifestyles (i.e. smoking and poor oral hygiene) influence the onset and progression of PD, but alone cannot cause it [4,5]. It is thought that about 50% of the probability of developing PD is related to heredity6. Clinical studies have shown that genetic factors are jointly responsible with environmental factors and lifestyles for the development of PD [2, 6-8].

Genetic susceptibility to multifactorial diseases is usually due to several gene polymorphisms instead of a single, or few, gene mutations. Common variation in the genetic code may results in altered expression or in functional changes of the encoded proteins, therefore resulting in an increase of disease severity or making individuals with genotypes more susceptible to a given disease [9].

Recently, investigations on susceptibility factors of periodontitis have mainly focused on genes that modulate immune regulation, such as cytokines, chemokines, cell-surface...
receptors, enzymes and proteins related to antigen recognition. Cytokines, such as IL-1α, IL-1β, IL-10, and IL-6, are key factors which mediate the inflammatory process during periodontitis progression. They have a role in activation, proliferation and differentiation of B cells that are the majority of infiltrating cells in advanced periodontitis lesions [10]. Thus, common variations in genetic code can alter the progression of disease [11] because they may be responsible for the repeated cycles of tissue inflammation [12].

In PD, the microbiota accumulated in the subgingival region is the environmental factors that influence the inflammatory response in periodontal tissues [13]. However, cytokines contribute to connective tissue destruction and bone resorption [14]. Another factor associated with bone resorption in periodontal disease is vitamin D receptor (VDR), which has been considered as a periodontitis susceptibility factor. ref Recent articles reported a revision of scientific literature regarding genetic association analysis between common polymorphisms of candidate genes and periodontitis [15,16].

It is noteworthy that the majority of the genetic studies on PD have employed small size cohorts, resulted in a large potential for false-positive and false-negative results, and thus had low statistical power to properly detect association. Additionally, the number and the types of disease-modifying genes in periodontal disease may be different in different ethnic populations or disease subgroups. Consequently only wide sample size - such as multicentric or national wide ones- can be sound. Instead pooling samples from different ethnic group (or nations) can make the study-group wiker since alleles can have different frequencies within each single ratial group.

Previous investigations have analyzed different polymorphisms between healthy and PD sites. This study allowed getting information about genetic markers of PD [17-18].

In order to test whether gene polymorphism acts as a susceptibility factors of PD in the Italian population, six specific polymorphism of the IL-1α, IL-1β, IL-6, IL10 and VDR genes in a big size cohort of more than 500 patients were recently investigated [19]. A statistical significant association between common variant alleles, IL6 rs1800795-G and IL 10 rs1800872-A, and periodontal disease was demonstrated. These data suggest a possible use of this polymorphism in a DNA-based diagnostic test of periodontitis (LAB-test®). Demmer et al.

Clinical use of genetic test for detecting PD

PD is a genetic disease influenced by environmental factors. ref Therefore, the identification of the main genetic markers can be a useful tool for early diagnosis since PD clinically arises in the middle age and therapy is today based on early clinical detection and hygiene control [14].

Patients with periodontally compromised parents may need prosthetic or implant-prosthetic treatment (PIT), and these patients have an increased risk of developing PD during their life. This is due both to oral hygiene which may be more difficult to maintain after PIT (which may lead to plaque accumulation and inflammation) and to genetic predisposition.

In periodontal disease, periodonto-pathogenic bacteria accumulated in the subgingival region are responsible for disease onset. The presence of prosthetic or implant-prosthetic apparatus increases the risk of accumulation of bacterial plaque and consequently of PD. Presence of fixed prosthesis and poor oral hygiene can allow periodontal bacteria to grow in plaque below the gum line, leading to changes in the microflora and progression from gingivitis to PD. A range of host genetic factors can influence individual susceptibility to periodontitis, and - among them - IL6 rs1800795-G and IL 10 rs1800872-A, are relevant.

Young patients with PIT are usually considered “healthy” people since they don’t have clinical signs of PD; however, they could have higher risk to develop PD and therefore compromise PIT in a short follow-up period. Hence, the use of a genetic test for identifying those with higher risk of PD is mandatory in order to guarantee a longer life-span to prosthetic work. These subjects should undergo to frequent oral hygiene recall to guarantee oral health and to prevent forensic litigation.

CONCLUSION

Oral rehabilitation presents many medico-legal concerns connected with the difficulties inherent to dental procedures and objectives (both functional and esthetic). An accurate assessment of each case by clinician is of paramount importance, and patients should receive complete information on the risk of the treatment, as well as possible limits and complications of the procedures. The successful outcome depends on scrupulous observance of the practitioner’s instructions and oral care. Thus, patient should be informed that if a poor oral hygiene follows oral rehabilitation, risk of PD is increased. In particular, it is recommended clinician perform genetic test aimed at identifying patients with higher genetic risk of PD. For those positive to the genetic test, a stricter oral hygiene program must be applied, including professional tooth cleaning and plaque control. It is likely that genetic analysis represents an effective and cheap method to rapidly predict patients with major risk of PD. From this point of view an association between common variant alleles, IL6 rs1800795-G and IL 10 rs1800872-A, and periodontal disease has been shown 19 and it can be used to detect high risk patients.

REFERENCES