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ORIGINAL ARTICLE

Association between monocyte chemoattractant protein-1 -2518 A/G gene polymorphism and the outcome of the nonsurgical periodontal treatment

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Genetic polymorphism;
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Abstract *Background/purpose:* Elevated monocyte chemoattractant protein-1 (MCP-1) is related to severe periodontal destruction. Furthermore, MCP-1 -2518 A/G gene polymorphism affects MCP-1 after inflammatory stimuli. This study analyzed the association between MCP-1 -2518 gene polymorphism and the outcome of nonsurgical periodontal treatment.
Methods: Forty periodontal patients were recruited and MCP-1 -2518 A/G gene polymorphisms were analyzed using polymerase chain reaction-restriction fragment length polymorphism assay. The clinical periodontal parameters, including probing depth (PD), clinical attachment level (CAL), gingival index (GI), bleeding index (BI) and plaque index (PI), were recorded before and six weeks after nonsurgical periodontal therapy. Patients were divided into chronic periodontitis (CP) or aggressive periodontitis (AP). Multiple linear regression analysis was performed to investigate certain predictors of the therapy outcome.
Results: The frequency of MCP-1 -2518 genotype-positive (carrying allele G) was 42.5%. Poor treatment outcome in PD, GI and BI improvement could be predicted with MCP-1 -2518 A/G genotype and aggressive periodontitis status as the predictor variables. In contrast, MCP-1 -2518 A/A genotype and aggressive periodontitis status could predict better treatment response in PD and BI improvement. However, MCP-1 -2518 genotype did not affect the treatment outcome in patients with chronic periodontitis.
Conclusion: MCP-1 -2518 A/G genotype might be useful in predicting less favorable nonsurgical treatment outcome in patients with aggressive periodontitis. However, MCP-1 -2518 gene

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polymorphism may not play a role in patients with chronic periodontitis. This study suggests that MCP-1 -2518 genotype may influence the outcome of nonsurgical periodontal treatment in aggressive periodontitis patients.

Introduction

Although periodontal diseases are initiated by oral bacteria, it is also evident that the host response plays a major role in the outcome of these infections. Chemokines are small signaling proteins which are involved in the physiology and pathophysiology of acute and chronic inflammatory processes, by attracting and stimulating specific subsets of leukocytes.[1] Monocyte chemoattractant protein-1 (MCP-1), also known as CC Chemokine Ligand-2 (CCL-2), is one of the important chemokine to initiate, regulate, and attract monocytes.[2] MCP-1 attracts chemokine receptor CCR2-positive cells.[3] MCP-1 expression in bacterially induced gingival inflammation is positively related to the degree of inflammation.[4] In addition, levels of MCP-1 in gingival crevicular fluid (GCF) were both higher in chronic periodontitis and aggressive periodontitis compared to the healthy control.[5,6] Pradeep et al. have found that MCP-1 levels in GCF and serum are positively related to the severity of periodontitis.[7,8] In the same studies, they have also investigated the effects of nonsurgical periodontal treatment on MCP-1 levels in GCF and serum. Significant reduction of MCP-1 levels has been observed in periodontal patients 6—8 weeks after treatment.

Smoking is a major risk factor for periodontitis.[9] Anil et al. have observed higher GCF levels of MCP-1 in smokers with periodontitis than nonsmokers with periodontitis and healthy control.[10] Tymkiw et al. have compared periodontitis sites to healthy sites in patients with periodontitis.[11] They have found that levels of MCP-1 in GCF are higher in diseased sites than healthy sites in nonsmokers while no difference in both sites in smokers. Haytural et al. have detected higher MCP-1 levels in serum in smokers with periodontitis than nonsmokers with periodontitis.[12] Smoking might have some effects on MCP-1 levels related to pathogenesis of periodontitis.

Polymorphisms in the regulatory region of MCP-1 gene, which increase the expression of MCP-1, have been demonstrated.[13] A biallelic A/G polymorphism has been found in the MCP-1 distal gene regulatory region at position -2518 (numbers indicate nucleotide positions relative to the major transcription start sites) that affects the level of MCP-1 expression in response to an inflammatory stimulus.[14] Monocytes from individuals carrying a G allele at -2518 produce more MCP-1 than monocytes from A/A homozygous subjects.[14] The MCP-1 -2518 A/G gene polymorphism appears as a genetic risk factor for myocardial infarction and cerebral infarction in two meta-analysis studies.[15,16] However, a study by Zhu et al. revealed that Chinese women with generalized aggressive periodontitis had lower frequency of MCP-1 -2518 A/G gene polymorphism than healthy female group (71.2% vs. 85.7%).[17] Their another research further studied combined effect of CCR2-V64I and MCP-1 -2518 A/G on aggressive periodontitis patients. They found the odds ratio for VV genotype (CCR2) and smoking, or MCP-1 (G genotype) and smoking were 7.4 and 4.9, respectively in male patients with periodontitis.[18]

Elevated MCP-1 is related to severe periodontal destruction. Significant reduction of MCP-1 levels has been observed in periodontal patients after nonsurgical periodontal treatment.[7,8] Furthermore, MCP-1 -2518 A/G gene polymorphism affects MCP-1 after inflammatory stimuli. However, the possible association between the genetic polymorphisms of MCP-1 and the outcome of nonsurgical periodontal treatments has not yet been investigated. The aim of the present study was to observe the frequency of the MCP-1 -2518 A/G polymorphism in the Taiwanese patients with periodontitis. The clinical parameters before and after nonsurgical periodontal treatment were also examined. Moreover, the association between the MCP-1 genotype and the outcome of non-surgical periodontal treatment in chronic and aggressive periodontitis patients was evaluated.

Materials and methods

Study population

A total of 40 participants with periodontitis were recruited from the patient pool at the Division of Periodontics, Department of Stomatology, Taipei Veterans General Hospital. Ethical approval for this research was approved by the Institutional Review Board of Taipei Veterans General Hospital. Demographic and personal data, including medical history, birth date, gender, family history, smoking status were collected. All participants were Taiwanese (19 male, 21 female; mean age: 46.88 $\pm$ 11.48) and met the following criteria: (1) no known systemic diseases or antibiotics/anti-inflammatory drug therapy in the previous three months; (2) not pregnant or breast feeding; (3) no periodontal treatment, including ultrasonic scaling, root planing, and periodontal surgery in the previous three months prior to the study, since healing following nonsurgical therapy is almost complete at three months.[19] Participants were all informed about the purpose and procedures and signed informed consent prior to entry into the study. The diagnostic criteria of periodontitis were based on clinical periodontal examination and full mouth periapical and bitewing radiographs. Baseline clinical parameters, probing depth (PD), clinical attachment loss (CAL), gingival index (GI),[20] bleeding index (BI),[20] plaque

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