Available online at www.sciencedirect.com

ScienceDirect

journal homepage: http://www.elsevier.com/locate/aob

Gingival crevicular fluid interleukin-36β (-1F8), interleukin-36γ (-1F9) and interleukin-33 (-1F11) levels in different periodontal disease

Sabri Fatih Kurşunlu [a], Veli Özgen Öztürk [a], Buket Han [b], Harika Atmaca [c], Gülnur Emingil [b,*]

[a] Department of Periodontology, School of Dentistry, Adnan Menderes University, Aydın, Turkey
[b] Department of Periodontology, School of Dentistry, Ege University, İzmir, Turkey
[c] Celal Bayar University, School of Science, Department of Biology, Manisa, Turkey

ARTICLE INFO

Article history:
Accepted 30 August 2014

Keywords:
Periodontal disease/pathogenesis
Gingival crevicular fluid
IL-33
IL-36β
IL-36γ

ABSTRACT

Background: Periodontal inflammation is driven by the coordinated action of a number of factors, including the IL-1 family. Our study aimed to examine the levels of interleukin (IL)-36β, IL-36γ and IL-33 levels in gingival crevicular fluid (GCF) from patients with different periodontal diseases.

Materials and methods: A total of 80 subjects, 20 patients with generalized aggressive periodontitis (G-AgP), 20 patients with chronic periodontitis (CP), 20 with gingivitis and 20 periodontally healthy subjects were included. Periodontal status was evaluated by measuring probing depth, clinical attachment loss, papillary bleeding index and plaque index. GCF cytokine levels were analysed by ELISA.

Results: CP, gingivitis and healthy groups had similar GCF IL-36β total amount ($p > 0.008$). G-AgP group had elevated IL-36β total amount compared to CP group ($p < 0.008$). G-AgP group had similar GCF IL-36β total amount to gingivitis and healthy groups ($p > 0.008$). GCF IL-36γ and IL-33 total amounts of the study groups were similar ($p > 0.05$).

Conclusions: The present study demonstrated for the first time the presence of IL-36β, IL-36γ and IL-33 GCF levels with different periodontal diseases. High levels of IL-36-β in the AgP group in comparison to CP group might suggest that periodontitis in the aggressive form could be related to the increase in GCF IL-36β.

1. Introduction

Periodontal disease results from complex interactions between microbial insult and the host inflammatory-immune responses, which involves both the innate and adaptive arms of the immune system.[1] The cross-talk between periodontal pathogens and inflammatory process is regulated by an orchestrated network of cytokines which are essential for most periodontal tissue breakdown, leading to clinical signs of disease.[2,3] The cytokine network takes control over inflammatory mechanisms in order to amplify or suppress tissue reactions in periodontal pathogenesis.[3,4]

* *Corresponding author at*: Ege Üniversitesi, Dişhekimliği Fakültesi, Periodontoloji Anabilim Dalı, Bornova-35100, I˙zmir, Turkey. Tel.: +90 232 3881105; fax: +90 232 3880325.
E-mail address: gemingil@yahoo.com (G. Emingil).
http://dx.doi.org/10.1016/j.archoralbio.2014.08.021

The interleukin (IL)-1 family of cytokines has a central role in triggering and perpetuating of immune and inflammatory responses.[5–7] They have been recently extended through the discovery of new IL-1 ligands, which were orphan ligands in the family for a long time.[7,8] These newly named cytokines IL-36α, IL-36β, and IL-36γ, previously known as IL-1F6, IL-1F8, and IL-1F9, have high amino acid sequence homology with IL-1β and IL-1ra proteins.[7,9–11] The genes encoding IL-36α, IL-36β, and IL-36γ are located on chromosome 2 in humans clustered with IL-1α, IL-1β and IL-1ra genes.[12–14] IL-36γ activates similar signaling pathways to those that regulate IL-1β including nuclear factor-kB (NF-κB) and mitogen-activated protein kinase (MAPK)-regulated transcription factors such as c-Jun-N-terminal kinase and extracellular signal-regulated kinases-mediated pathways on binding to receptor complex called IL-1Rrp2 (IL-36R) and IL-1RAcP and this action is blocked by IL-36Ra (IL-1F5) which acts as an IL-36R antagonist.[15] In addition to IL-36γ, IL-36β has also been reported to trigger MAPKs and NFκB signaling via similar mechanism present and active in epithelia.[16]

The recent expansion of the IL-1 family has opened up areas for further elucidating the pathways of IL-1 actions in different systemic diseases.[5–7,17] IL-36β induces the production of inflammatory cytokines such as IL-6 and IL-8 and amplifies neutrophilic inflammation.[15,16,18] IL-36γ acts as a proinflammatory cytokine during inflammation.[19] They can regulate the expression and enhance the function of Th17 cytokines besides being induced by these cytokines.[20,21] IL-36 cytokines are potent activators of Th1 responses, stimulate cytokines production by dentritic cells and act critical role between innate and adaptive immunity.[22]

IL-33, also known as IL-1F11, was originally identified as a nuclear factor in high endothelial venules.[23] IL-33 is now recognized as a dual- function cytokine acting both as a traditional cytokine through activation of the orphan receptor ST2 of the Toll-like receptor/IL-1R superfamily.[7,24] It is also an intracellular nuclear factor with transcriptional regulatory properties localized to the nucleus.[25,26] It affects specific T cell populations, inducing production of cytokines from Th2 cells in addition to the regulation of innate immune response, particularly via mast cell activation.[17,24,27] IL-33 is released by damaged cells, acting as a danger signal to alert cells of the innate immune system during infection.[27,28] Therefore, IL-33 has been proposed as an alarmin-like molecule.[29] It has a dual-function having an intracellular function as well as mediating pro-inflammatory responses as an extra-cellular cytokine.[23,25,28,30]

New data are emerging regarding the role of these novel cytokines in several inflammatory diseases.[17,31–34] Owing to their ability to activate cells of both the innate and adaptive immune system, novel cytokines might provide valuable insights into the mechanisms involved in the initiation and progression of periodontal diseases. To date, little is known concerning the role of IL-33 in periodontal disease and IL-36 cytokines have not yet been investigated in periodontal disease.[35–37] Therefore, the present study aims to investigate the presence of IL-33, IL-36β and IL-36γ in gingival crevicular fluid (GCF) samples of patients with different periodontal disease and to test whether they are correlated with clinical parameters.

2. Materials and methods

2.1. Study population

A total of 80 subjects were included in this study. All consecutive subjects were recruited from the Department of Periodontology, School of Dentistry, Ege University, İzmir, Turkey. The study was approved by the Ethics Committee of the Medical Faculty of Ege University and was conducted according to the guidelines of the Declaration of Helsinki. Written and informed consent was obtained from each patient before enrolment in the study. The purpose of the study was completely explained to each subject before entering the study and informed consent was obtained from each subject. Complete medical and dental histories were taken from all subjects. All of the patients were non-smokers, had at least 20 teeth in the mouth. None of the subjects had a history of systemic disease and had received antibiotics or other medications or non-surgical/surgical periodontal treatment within the past 4 months. Patients with severe medical disorders including diabetes mellitus, immunological disorders and pregnant females were excluded from the study. The selection of the patients was made according to the clinical and radiographic criteria proposed by the 1999 International World Workshop for a Classification of Periodontal Disease and Conditions.[38]

Generalized aggressive periodontitis group (G-AgP). The G-AgP group included 10 females and 10 males ranged in age from 20 and 38 with a mean age of 30.0 ± 5.0 years. These patients demonstrated a generalized pattern of severe destruction and clinical attachment loss (CAL) of ≥ 5 mm on 8 or more teeth; at least 3 of those were other than central incisors or first molars which was not commensurate with the amount of plaque accumulation or local contributing factors.

Generalized chronic periodontitis group (CP). The CP group consisted of 11 females and 9 males between the ages of 30 and 61 (mean of 44.1 ± 7.8 years). They had moderate to severe alveolar bone loss and CAL of $\geq$5 mm and probing depth (PD) of ≥ 6 mm in multiple sites of all four quadrants of the mouth which was commensurate with the amount of plaque accumulation.

Gingivitis group. The gingivitis group included 11 females and 9 males with varying degrees of gingival inflammation, but no signs of CAL were observed. These patients ranged in age from 22 to 56 (mean age 38.1 ± 11.3 years).

Healthy group. The healthy group consisted of 10 females and 10 males who exhibited PD < 3 mm and no CAL, clinical inflammation, sulcular bleeding and radiographic evidence of bone loss (mean age 40.9 ± 6.2 years; range 32–52 years). These individuals were healthy volunteers from the Department of Periodontology.

2.2. Determination of periodontal status

At the screening stage, to determine the clinical periodontal status, all subjects had a clinical periodontal examination including the measurement of PD and CAL by one examiner (B.H). The plaque index (PI) and papillary bleeding index (PBI) were also recorded.[39,40]