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RESEARCH ARTICLE

Salivary and serum interleukin-17A and interleukin-18 levels in patients with type 2 diabetes mellitus with and without periodontitis

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Abstract

Objective

Interleukin (IL)-17A and IL-18 have been proposed to play important roles in periodontitis and type 2 diabetes mellitus (DM), but human data are conflicting. The present study aimed to investigate the roles of IL-17A and IL-18 in periodontitis and DM by measuring salivary and serum levels, respectively.

Materials and methods

A total of 49 participants with type 2 DM and 25 control subjects without type 2 DM were recruited. A periodontal screening and recording (PSR) index (0, 1–2, 3, and 4) was used to classify whether these subjects had periodontitis. Salivary and serum IL-17A and IL-18 levels were measured by enzyme-linked immunosorbent assay. Multiple linear regression analyses were used to evaluate the associations between these cytokines and clinical parameters.

Results

Salivary IL-17A levels were not significantly different between patients with DM and controls, however, the levels were significantly higher in controls with periodontitis than those without periodontitis ($p = 0.031$). Salivary IL-17A levels were significantly associated with the PSR

committee of the Faculty of Medicine, Chulalongkorn University. Data will be available from the Faculty of Medicine, Chulalongkorn University Institutional Data Access / Ethics Committee (contact via Miss Suwanna Muanpetch, aumaim44@hotmail.com) for researchers who meet the criteria for access to confidential data.

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index ($\beta = 0.369$, $p = 0.011$). Multiple linear regression analyses revealed the association of salivary IL-18 levels and fasting plasma glucose ($\beta = 0.270$, $p = 0.022$) whereas serum IL-18 levels were associated with HbA_{1C} ($\beta = 0.293$, $p = 0.017$). No correlation between salivary and serum levels of IL-17A and IL-18 was found.

Conclusion

Salivary IL-17A was strongly associated with periodontitis, whereas salivary IL-18 was associated with FPG and serum IL-18 was associated with HbA_{1C}. These results suggest the role of these cytokines in periodontal inflammation and DM.

Introduction

A close relationship between diabetes mellitus (DM) and periodontitis has long been recognized [1]. Patients with DM have an increased risk to develop periodontitis and those with untreated periodontitis seem to have a poorer glycemic control. Possible mechanistic links between DM and periodontitis have been proposed, including altered polymorphonuclear cell (PMN) function, increased adipokine production, and altered apoptosis, which could result in increased inflammatory cytokine production in both patients with periodontitis and DM [1]. Recent studies have identified inflammation as an important factor in the pathogenesis of DM [2, 3]. In clinical studies, increased levels of several pro-inflammatory cytokines including tumor necrosis factor-α (TNF-α), interleukin (IL)-1, IL-6, and IL-18 were associated with various diabetic complications [4–6].

Local inflammation inevitably underlies the pathological basis of periodontitis. T-helper (Th) 17 cells, the recent subset of T-cells, were shown to be relevant to the pathogenesis of periodontal disease since increased Th17 cells in inflamed gingival tissue of periodontitis patients was demonstrated [7]. IL-17A is the most studied member of the Th17 cytokine family and its overproduction was related to autoimmune diseases and chronic inflammation, including periodontitis [8, 9]. IL-17A has been suggested to contribute to the pathogenesis of periodontitis in many ways. First, it can induce the receptor activator of nuclear factor κB (RANK)—RANK ligand (RANKL) signaling pathway which promotes osteoclastogenesis [10, 11]. Second, it acts as a regulatory cytokine that induces inflammatory responses by stimulating the release of other inflammatory cytokines including IL-6, IL-8, and IL-1β from macrophages, epithelial, and fibroblastic cells [11]. Third, it participates in regulating some matrix metalloproteinases (MMPs) production that could lead to periodontal tissue destruction [12]. Th17 cells have been proven as the main source of IL-17 in both healthy and diseased gingiva [13]. Other cells in periodontal tissues, including macrophages, mast cells, neutrophils, natural killer T (NKT) cells, gamma-delta (γδ) T-cells, and periodontal ligament cells can also produce this pro-inflammatory cytokine [14]. Therefore, periodontal inflammation could induce increased IL-17 levels. In addition, IL-18, a member of IL-1 family, is a potent inflammatory cytokine that regulates the inflammatory process by stimulating Th1 or Th2 responses. It can stimulate Th1 synergistically with IL-12 and results in the production of interferon-gamma (IFN-gamma) [15]. IL-18 is produced in various cell types, including endothelial cells, vascular smooth muscle cells, macrophages, dendritic cells, and adipocytes. It has also been suggested to be involved in periodontal inflammation since elevated IL-18 levels in gingival crevicular fluid (GCF) and saliva were found in patients with chronic periodontitis [16, 17].

Nevertheless, recent studies reported conflicting results regarding the roles of IL-17A and IL-18 in periodontal disease. Awang *et al.*[18] revealed significantly higher IL-17A levels in