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Review article

Cytokine profile in the synovial fluid of patients with temporomandibular joint disorders: A systematic review

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ABSTRACT

The aim of this study was to review the cytokine profiles in the synovial fluid (SF) of patients with temporomandibular joint disorders (TMJD). Databases were searched from 1965 till September 2015 using different combinations of the following key words: "Temporomandibular joint"; "Cytokine"; "disorder"; and "synovial fluid" and "inflammation". Titles and abstracts of studies identified using the above-described protocol were screened and checked for agreement. Full-texts of articles judged by title and abstract to be relevant were read and independently evaluated. Hand-searching of the reference lists of potentially relevant original and review articles was also performed. The pattern of the present systematic review was customized to mainly summarize the relevant data. Fifteen studies were included. In 12 studies, cytokine profile of patients with TMJD was assessed using enzyme linked immunosorbent assay; and in 2 studies, histological analysis was performed to assess the cytokine profile of patients with TMJD. Patients with TMJD presented raised levels of interleukin (IL)-6 in 8 studies, IL-1beta (1β) in 5 studies and tumor necrosis factor-alpha (TNF-α) in 5 studies. Two studies showed no significant difference in TNF-α levels in patients with and without TMJD; and IL-1β levels were comparable in patients with and without TMJD in 2 studies. Raised levels of IL-6, TNF-α, IL-1β, IL-8, and IFN-γ in the SF have been associated with inflammation in patients with TMJD. Cytokines IL-10, osteoclastogenesis inhibitory factor/osteoprotegerin (OCIF/OPG), and VEGF found in the SF of TMJs could have an anti-inflammatory effect.

Contents

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1. Introduction

Temporomandibular joint disorders (TMJD) are characterized by muscle-skeletal conditions and craniofacial pain in the masticatory system involving the joint, masticatory muscles or muscle innervations. Factors that have been associated with the etiology of TMJD include growth and developmental anomalies [1], trauma [2], detrimental body posture [3], parafunctional habits and bruxism [4], and stress [5]. Disc internal derangement (characterized by abnormal anatomic relationship between the articular disc and the articulating surfaces) and osteoarthritis (abnormal anatomic relationship between the articular disc and the articulating surfaces abnormal anatomic relationship between the articular disc and the articulating surfaces) are the most common forms of TMJD [6].

The degenerative changes in the TMJ are associated to osteoclastogenesis [7], however the molecular process associated to these changes are unclear. Studies [8–11] have shown that concentrations of monocyte-macrophage derived cytokines are raised in the synovial fluid (SF) of patients with TMJD. It has been reported that cytokines such as (interleukin [IL]-1beta [β], IL-6 and tumor necrosis factor-alpha [TNF-α]) may promote the release of proteinases and stimulate the expression of degrading enzymes and inflammatory mediators, resulting in TMJ inflammation and bone and cartilage degradation [12]. These results indicate a possible role of cytokines in the pathogenesis of TMJD. Recent studies [13–15] have suggested that the alteration of osteoprogeterin (OPG) and factor-kappa B ligand (RANKL) ratio can induce bone-destructive diseases like periodontal disease and rheumatoid arthritis. Wakita et al. [16], suggested a decrease in the concentration of OPG, in contrast to an unchanged concentration of RANKL in the SF from patients with TMJD. Other inflammatory mediators, bone-destruction associated cytokines and metallo-proteinases (MMPs) have been associated to TMJD, including: Interferon-gamma (IFN-γ), Prostaglandin E_2 (PGE_2), IL-17, MMP-2, MMP-9, aggrecanase-1 and aggrecanase-2 [8,9,17–19]. Therefore, the cytokine equilibrium, including their receptors and receptor antagonist are key factors for the beginning, progression and clinical expression of TMJDs. It is pertinent to systematically review the cytokine profile in the SF of patients with TMJD in an attempt to appraise the immunological biomarkers expressed in the SF of patients with TMJD. Hence, the aim of the present systematic review was to determine the cytokines profile in the SF of patient with and without TMJD.

2. Materials and methods

2.1. Focused question

Based on the Preferred Reporting Items for Systematic Review and Meta-analysis (PRISMA) guidelines, a specific question was constructed. The focused question addressed was "Is there a difference in the cytokines profile in the SF of patients with and without TMJD?"

2.2. Eligibility criteria

The following eligibility criteria were entailed: (a) original clinical studies; (b) patients with TMJD; (c) inclusion of control group; and (d) intervention: patients with and without TMJD. Letters to the editor, historic reviews, case reports, case-series and unpublished articles were excluded.

2.3. Search strategy and study selection

PubMed/Medline (National Library of Medicine, Washington, DC), EMBASE, Scopus, Web of knowledge and Google-Scholar databases were searched from 1965 up to and including September 2015 using the following combination of keywords; (a) temporomandibular joint disorder + cytokines + synovial fluid; (b) temporomandibular joint disorder + cytokines + synovial fluid + inflammation; (c) disc internal derangement + temporomandibular joint + cytokines + synovial fluid; (d) interleukin + temporomandibular joint disorders + inflammation; (e) interleukin + temporomandibular joint disorders + inflammation + synovial fluid; (f) tumor necrosis factor alpha + temporomandibular joint disorders + inflammation; (g) tumor necrosis factor alpha + temporomandibular joint disorders + inflammation + synovial fluid; (h) osteoarthritis + temporomandibular joint disorders + inflammation; (i) osteoarthritis + temporomandibular joint disorders + inflammation + cytokines + synovial fluid.

Titles and abstracts of studies identified using the above-described protocol were screened by two authors (SVK and FV) and checked for agreement. Full-texts of studies judged by title and abstract to be relevant were read and independently evaluated for the stated eligibility criteria. Reference lists of potentially relevant original and review articles were hand-searched to identify any studies that could have remained unidentified in the previous step. Once again, the articles were checked for disagreement via discussion among the authors (Fig. 1).

The initial search yielded 33 studies. Eighteen studies, which did not fulfill the eligibility criteria, were excluded (see Appendix A). In total, 15 studies [6,11,16,20–31] were included and processed for data extraction (Tables 1 and 2).

2.4. Methodological study quality assessment

The Newcastle–Ottawa Scale [32] (NOS) was used to grade the methodological quality of each study assessed in the present systematic review. In summary the NOS scale uses a systematic approach based on 3 specific criteria: Selection (S), Comparability