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Tumor necrosis factor-alpha levels in the synovial fluid of patients with temporomandibular joint internal derangement

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ABSTRACT

Purpose: The purpose of this study was to investigate the level of tumor necrosis factor-alpha (TNF-α) in the synovial fluid (SF) of patients with temporomandibular joint (TMJ) internal derangement and to show the relationship between the level of TNF-α and the severity of the disease.
Materials and methods: Arthrocentesis was performed on 32 female and five male patients (aged between 17 and 45) referred to our clinic with the complaint of TMJ pain and discomfort. TNF-α levels were determined in the SF samples obtained during arthrocentesis. As a measure of pain, visual analog scale (VAS) scores were also evaluated.
Results: There were statistically significant differences in VAS scores between the stages. VAS scores were found to be elevated as the stage of disease progressed. Increased levels of TNF-α were found in progressive stages of internal derangement.
Conclusion: In our study, both SF TNF-α levels and pain levels (VAS scores) were found to be increased in patients with internal derangement as the stage of the disease progresses. TNF-α might contribute to the pathogenesis of synovitis and the degeneration of the TMJ cartilage and bone.

1. Introduction

Internal derangement of the temporomandibular joint (TMJ) is defined as an abnormal anatomic relationship between the articular disc and the articulating surfaces (Emshoff and Rudisch, 2007). Clinically, internal derangement is characterized by jaw pain, clicking of the joint, irregular and limited jaw motion, or restriction of joint function during mandibular movement. Whether any dysfunction is accompanied by pain depends on the adaptive capacity of the patient (Güven et al., 2007). TMJ osteoarthrosis (OA) which leads to TMJ pain and dysfunction is characterized by hard tissue destruction and degenerative changes. Internal derangement of the TMJ and OA are closely related entities (Emshoff et al., 2000; Kim et al., 2012a, 2012b).

In recent years, composition of the synovial fluid (SF) and reports about biochemical changes have provided new insights into the pathogenesis of TMJ diseases. Synovial fluid from the TMJ has been analyzed for the presence of various mediators, proinflammatory cytokines and free radicals (Hamada et al., 2008; Sicurezza et al., 2013).

It is thought that proinflammatory cytokines, such as interleukin-1 (IL-1), tumor necrosis factor-α (TNF-α) and interleukin-6 (IL-6) in synovial fluid may be related to the pathogenesis of synovitis and degenerative changes of the TMJ (Kaneyama et al., 2002).

TNF-α is a pleiotropic cytokine that is produced by a number of cell types, including activated macrophages and monocytes. It is a major mediator of immune regulation and inflammatory response (Nordahl et al., 2000). Overproduction or inappropriate expression of TNF-α can lead to a variety of pathological conditions (Feldmann et al., 1996; Kaneyama et al., 2005). The biological effects of TNF-α occur subsequent to its binding to specific cell surface receptors (Roux-Lombard et al., 1993; Kaneyama et al., 2005). It has been shown to selectively decrease the production of cartilage collagens and to suppress aggregating proteoglycan synthesis while promoting tissue degradation (Saklatvala, 1996). TNF-α has been detected in the synovium and SF of patients with internal

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derangement and OA (Sandler et al., 1998; Takahashi et al., 1998; Nordahl et al., 2000). There are very few studies reporting the possible involvement of TNF-α in the severity of internal derangement. On the other hand, to our knowledge, TNF-α levels have not been investigated in the SF of TMJs.

The aim of the present study was to investigate the level of TNF-α in the SF of patients with TMJ internal derangement, and the possible relationship between the level of TNF-α and the severity of the disease.

2. Materials and methods

This study included 32 female and 5 male patients aged between 17 and 45 (30.46 ± 2.56) who were referred to the Department of Oral and Maxillofacial Surgery, Faculty of Dentistry, University of Ankara between July 2007 and March 2010 with the complaint of pain around TMJ area. After detailed examination, patients were diagnosed with internal derangement. Exclusion criteria were systemic arthropathy, use of nonsteroidal antiinflammatory drugs and/or a history of trauma. This study was approved by the local ethics committee of the Ankara University Faculty of Dentistry, and informed consent was received from the patients before the procedure.

To attain a consistent surgical procedure and treatment protocol, surgical interventions were performed by the same clinician (OG). All patients who underwent arthrocentesis fulfilled a visual analog scale (VAS) to assess pain with endpoint marked scores of 0 (no pain) and 100 (worst pain). The maximum interincisal opening (MIO) was measured with a ruler to the nearest millimeter. Joint movements were investigated by finger palpation. Magnetic resonance (MR) of the TMJ was used for diagnosis. The preoperative clinical signs of the patients are shown in Table 1.

Table 1
Patient background data.

Wilkes classification	Age(yrs)	Gender	Disease side	TNF-α(pg/ml)	VAS	MIO(mm)
Stage III	28	F	R	17	74	23
Stage III	29	F	L	21.4	74	17
Stage III	28	F	R	18.4	79	15
Stage III	29	F	L	20.8	80	12
Stage III	35	F	R	18.9	75	10
Stage III	20	F	R	16.5	69	25
Stage III	40	M	R	18.6	74	20
Stage III	30	F	R	18.1	69	6
Stage III	30	M	L	16.2	75	18
Stage III	40	F	L	16.8	73	27
Stage III	33	F	R	10.5	68	4
Stage IV	18	F	L	22.7	80	15
Stage IV	19	F	R	24.1	78	24
Stage IV	38	F	R	23.5	83	17
Stage IV	39	F	R	19.2	88	18
Stage IV	41	F	L	25.4	78	14
Stage IV	30	F	L	28.1	71	10
Stage IV	17	F	R	28.6	79	19
Stage IV	29	F	R	27	80	20
Stage IV	23	M	L	26.8	76	15
Stage IV	19	F	R	25.1	77	24
Stage IV	30	F	L	18.1	84	23
Stage IV	43	F	L	24.1	77	24
Stage IV	23	F	R	22.2	81	16
Stage IV	45	F	R	27.3	73	22
Stage V	22	F	R	30.8	85	22
Stage V	20	F	R	32.7	86	21
Stage V	31	F	R	32.4	91	14
Stage V	22	F	L	35.4	89	23
Stage V	32	F	R	32.4	81	21
Stage V	40	F	L	37.3	81	22
Stage V	32	F	R	27.3	82	19
Stage V	37	M	L	33	85	22
Stage V	35	F	R	26.8	75	31
Stage V	32	M	L	27.3	86	22
Stage V	37	F	L	36.8	84	24
Stage V	31	F	R	32.4	86	17

Abbreviations: F: Female; M: Male; MIO: Maximum interincisal opening; VAS: Visual analog scale (0–100).

The results of radiological and clinical findings were classified according to Wilkes classification (Wilkes, 1989) as follows. Stage I (early stage): No significant mechanical symptoms, no pain or limitation of motion. Stage II (early-intermediate stage): First few episodes of pain, occasional joint tenderness and related temporal headaches, increase in intensity of clicking, joint sounds later in opening movement, beginning transient subluxations or joint locking. Stage III (intermediate): Multiple episodes of pain, joint tenderness, temporal headaches, locking, closed locks, restriction of motion, painful chewing (characteristic), anterior disc displacement, moderate to marked disc thickening, normal osseous contour (imaging). Stage IV (intermediate-late): Chronic and episodic pain, headaches, variable restriction of motion (characteristic), anterior disc displacement, marked disc thickening and abnormal bone contours (imaging). Stage V (late): Crepitus on examination (characteristic), variable and episodic pain, anterior disc displacement with disc perforation and gross deformity, degenerative osseous changes (imaging), chronic restriction of motion and difficulty with function.

The TMJ arthrocentesis procedure was performed as described by Nitzan et al. (1991). Before arthrocentesis for the collection of synovial fluid, 2 ml saline solution was injected into the superior joint compartment after subcutaneous local anesthetic administration (3% Citanest Octapressin solution containing prilocaine hydrochloride 30 mg/mL, Dentsply, Surrey, UK). To allow the saline solution to mix with the SF, the solution was aspirated and then reinjected 5 times, and the mixed solution was aspirated for the biochemical analysis. None of the samples were hemorrhagic. The synovial fluid samples were kept frozen at −80 °C. Because of ethical reasons and restrictions, the study was performed without control samples.

Synovial fluid TNF-α levels were measured by a commercial ELISA kit (TNF-α [human] ELISA Kit; Cayman Chemical Company, USA). The assay is an immunometric (sandwich) assay which permits TNF-α measurements within the range of 0–250 pg/ml, with a detection limit of 3.9 pg/ml.

3. Results

Thirty seven patients who had undergone arthrocentesis were grouped according to Wilkes classification: 11 patients were stage III (9 female and 2 male, mean age 31.09 ± 3.86 years), 14 patients were stage IV (13 female and 1 male, mean age 29.57 ± 5.8 years), and 12 patients were stage V (10 female and 2 male, mean age 30.92 ± 4.09 years). There were no statistically significant differences in ages between the stages ($P > 0.05$). There were no statistically significant differences in MIO between the stages (stage III: 16.09 ± 5.07; stage IV: 18.64 ± 2.54; stage V: 21.50 ± 2.59)

Table 2
TNF-α levels in the TMJ synovial fluid of patients with internal derangement classified according to Wilkes.

Stage	TNF-α (pg/ml)
III ($n = 11$)	17.52 ± 1.92*
VI ($n = 14$)	24.44 ± 1.82*
V ($n = 12$)	32.05 ± 2.25*

*$P < 0.05$ (Mean ± SD).