

The Evaluation of sIL-1RII, sTNF- α RI and sIL-6R Concentrations in Synovial Fluid in Patients with Temporomandibular Joint Derangements and affects on Success of Arthrocentesis

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Abstract: Background: The effects of proinflammatory cytokines have been shown as the cause of temporomandibular joint disorders (TMD). Especially, IL-6, TNF- α , IL-1 and their receptors are noticeable. Aim: The study aimed to evaluate sIL-1RII, sTNF- α RI and sIL-6R concentrations in synovial fluid of the patients with TMD and to determine the effect of these receptors on the success of arthrocentesis. Material and Methods: In this study the synovial fluid samples of 23 patients with complaint of limited mouth opening and pain, who underwent arthrocentesis were examined. Maximum mouth openings of each patient were measured before, at the 1st week and on the 1st month of operation. Visual Analog Scale (VAS) was used for measuring pain. For each receptor ELISA kits were used. Results: The concentrations of sIL-1RII and sTNF- α RI in the successful group were not different from the unsuccessful group, but the concentrations of sIL-6R and total protein concentration in successful group was higher than the unsuccessful group ($p < 0.05$). The success of the arthrocentesis was 65.2% unsuccessful and 34.8% successful at postoperative 1st month. Conclusions: sIL-6R and high protein concentration in the synovial fluid may be effective, but sTNF- α RI and sIL-1RII may not be effective in the success of arthrocentesis.

Keywords: Temporomandibular joint derangements, cytokines, arthrocentesis

1. Introduction

Temporomandibular joint (TMJ) internal derangements (ID) are defined as internal structure irregularities between condyle and articular eminens [1]. Closed locking (CL) is the most serious form of TMJ ID [2]. Trauma, excessive functional loading, degenerative joint changes and occlusal problems are important factors in the pathogenesis of TMJ ID [3]. Clinical signs of CL include muscle spasm, limited mouth opening, pain and clicking and TMJ arthrocentesis is frequently used to reduce these complaints [2]. This locking of jaw was thought to be related to the disk position, however, in recent years, the change in synovial fluid caused by proinflammatory cytokines like IL-6, TNF- α , IL-1 β and TMJ cartilage degeneration is thought to be factored in the etiology of CL [4,5].

Cytokine receptors are divided into two, bound and free. Free receptors like sIL-1RII and sTNF- α RI compete with cytokines to suppress the effects of cytokines, whereas only sIL-6R is contrary to this situation and affects the IL-6 molecule in an agonist direction [6].

Although there are many studies in the literature on the effect of proinflammatory cytokines such as IL-6, TNF- α and IL-1 β on TMJ internal disorder [7,8], there are few studies on the effect of soluble receptors of these cytokines on TMD and on the success of arthrocentesis.

The clinician may not have any predictions regarding the prognosis of the treatment when performing TMJ arthrocentesis treatment, and cannot determine the healing

potential after performing this treatment, whereas knowing the amount of specific cytokine receptors in the synovial fluid may be a predictor and predictor of treatment success.

The aim of this study was to evaluate sIL-1RII, sTNF- α RI and sIL-6R concentrations in synovial fluid of the patients with TMD and to determine the effect of these receptors on the success of arthrocentesis.

2. Material and Methods

This study was performed with 23 patients (21 female and 2 male) with complaint of limited mouth opening and pain during jaw functions, attending to the Oral and Maxillofacial Surgery Clinics of Faculty of Dentistry, Ankara Baskent University. All patients were diagnosed with TMJ anterior disk displacement without reduction clinically and radiologically.

Patients without any systemic disease to contraindicate to the procedure and who were not exposed to major trauma to the jaw region were selected for this study. All the patients had limited mouth opening. The patients who had complaints due to intraarticular structures were included in the study and the diagnosis was supported by Magnetic Resonance Imaging.

The main complaints of the patients, initial symptoms, duration of complaints, bruxism, presence of the voice in the joint during the opening and closing movements of the jaw, and the presence of deviation was recorded.

Maximum mouth opening was determined by measuring the distance between the upper and lower central teeth with a caliper preoperatively, immediately after the arthrocentesis procedure, postoperative 1st week and 1st month. The degree of pain occurring in the palpation of the preauricular region was assessed by the Visual Analog Scale (VAS) test.

In addition VAS values (0 = none, 10 = severe) and shaped pain scale values (0 = none, 1 = very little, 2 = slightly, 3=more, 4 = too much pain, 5 = too much pain to be treated) were measured preoperatively and postoperative 1st week and 1st month.

Arthrocentesis technique

Before the operation maximum mouth openings were measured in all patients. Two points were identified in front of tragus 1 and 2 cm along the canthal and tragus line, similar to the entry points used in the arthroscopic procedure on the fossa and eminens [9].

Auriculotemporomandibular nerve was blocked with 2 ml of local anesthetic solution (ultracain ds forte^R- 40 mg/ml articain HCL, 0.0012 mg/ml ephineprin) and entered the upper joint cavity with a 20 gauge needle.

Superior joint space was inflated with approximately 2 ml of sterile saline solution. The patient was asked to open and close his or her mouth for several times to mix the saline solution and synovial contents. Then intra-articular fluid was transferred back into the syringe with negative aspiration. Aspiration and injection was repeated 10 times without draining this liquid from the syringe. After aspiration of this resulting synovial fluid sample, the temporomandibular joint space was washed with a single needle. Then, arthrocentesis procedure was continued using a second needle. The procedure was completed using approximately 400 ml saline solution.

Non-steroidal anti-enflamatuar drug usage was stopped 1 week before to prevent changes in cytokine levels in the synovial fluid. The success criteria of the treatment success was determined with MMO \geq 38 mm and a reduction in VAS scores.

Preperation of Synovial Fluid Sample

All samples were diluted by 1/20 ratio. The total fluid volume of samples were 2.1ml. Samples were centrifuged at 2500 rpm for 10 minutes and stored at -20°C until biochemical analysis.

Soluble human tumor necrosis factor receptor (sTNF- α RI) ELISA kit (Biosource international inc. Robert Maciel Associates, Massacuset, USA), interleukin- 6 receptor ELISA kit (Biosource International inc. Camarillo, California, USA) and human sIL-1RII ELISA kit (HyCult Biotechnology, USA) were used in synovial fluid samples for measurement of sTNF- α RI, sIL-6R and sIL-1RII, respectively. Total protein concentrations were measured by ROCHE Modular PP (Roche, France). Examination kits were studied as described in the manufacturer's package insert.

Statistical analysis

In the data analysis stage, first the general profile of the study group was created by using descriptive statistics using SPSS 25.00 package program. In the analysis part of the study, whether the success and unsuccess of the cases was statistically significant between concentrations of the proinflammatuar receptors (s IL-6R (pg / ml), sTNF α -RI (ng/ml), sIL-IRII (ng / ml)) and total protein concentrations samples were analyzed with Student t-test ($p < 0.05$).

3. Results

Table 1: Evaluation of VAS and MMO

| | Mean | Minimum | Maximum | Variance |
|----------------------------------|------------------|---------|---------|----------|
| Pre-op VAS | 5.78 \pm 1.76 | 3 | 9 | 3.087 |
| Pre-op MMO/ mm | 22.06 \pm 2.42 | 18 | 26 | 5.848 |
| PO 1 st week VAS | 2.22 \pm 1.126 | 0 | 5 | 1.269 |
| PO 1 st week MMO/mm | 37.87 \pm 2.22 | 33.8 | 42 | 4.91 |
| PO 1 st month VAS | .91 \pm .85 | 0 | 3 | .719 |
| PO 1 st month MOO/ mm | 36.30 \pm 2.68 | 31 | 40 | 7.18 |

Values represent mean \pm SD.

(* $p < 0.05$)

Table 2: Concentrations of proinflammatory cytokine receptors and total protein in synovial fluid

| | Mean | Min | Max | Successful treatment | Unsuccessful treatment | p |
|-----------------------------|-------------------|-------|--------|----------------------|------------------------|--------|
| sIL-6R (pg/ml) | 17.30 \pm 12.65 | 4.685 | 54.576 | 42 \pm 4.57 | 21.50 \pm 13.66 | 0.025* |
| sTNF α -RI (ng / ml) | 0.34 \pm 0.27 | 0.095 | 0.919 | 0.35 \pm 0.27 | 0.33 \pm 0.28 | 0.834 |
| sIL1-RII (ng / ml) | 6.84 \pm 5.52 | 1.44 | 23.98 | 10.20 \pm 8.02 | 5.05 \pm 2.43 | 0.290 |
| Total protein (μ g/ml) | 24.20 \pm 21.26 | 3.1 | 84.2 | 6.67 \pm 4.49 | 33.55 \pm 20.76 | 0.02* |

Values represent mean \pm SD.

(* $p < 0.05$)

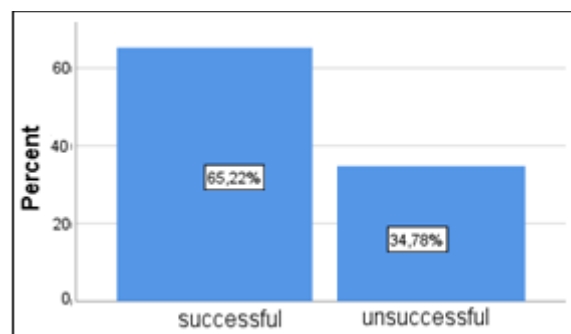


Figure 1: Results of 1st month arthrocentesis treatment success

A total of 23 patients, 21 females (91.3%) and 2 males (8.7%) were included in present study. Ages were ranged from 17 to 57 years (mean 35.65 \pm 12.78). In the descriptive statistics of VAS values, the mean preoperative VAS values of 23 patients were 5.78, 1st week VAS median 2.22 and 1st month VAS median 0.91 (Table 1).

The preoperative mouth openings in all patients were measured, we found that patients had preoperative MMO of 18-26 mm (mean 22.06 \pm 2.42 mm), and a mean of 33.8-42.0 mm (mean 37.87 \pm 2.22mm) at postoperative 1st week. Also, MMO at 1st month decreased to 31-40 mm (mean

36.3±2.68mm) (Table 1). The mouth openings were significantly increased after 1st week and month ($p < 0.05$) however, a statistically significant decrease was observed when the mouth openings were compared at the postoperative 1st week and at the postoperative 1st month ($p < 0.05$) (Table 1).

sIL-6R concentrations of all patients in synovial fluid samples were 4.685-54.576 pg / ml (mean 17.30±12.65 pg/ml), whereas sTNF α -RI concentrations were 0.095-0.919 ng / ml (mean 0.34± 0.27 ng/ml). sIL-1RII concentrations were 1.440-23.978 ng / ml (mean 6.84± 5.52 ng/ml), while total proteins concentration were 3.1-84.2 μ g/ml (mean 24.20± 21.26 μ g/ml) (Table 2).

The mean sIL-6R in the synovial fluid sample of the successful group was 9.42±4.57 pg/ml, whereas it was 21.50±13.66 pg/ml in the unsuccessful group so it was statistically significant difference between two groups ($p < 0.05$). Since the mean sTNF α -RI in the successful group was 0.35± 0.27 ng/ml it was found to be 0.33± 0.28 ng/ml in the unsuccessful group and the difference was not significant ($p < 0.05$). sIL-1RII was determined as 10.20± 8.02 ng/ml in the successful group and 5.05±2.43 ng / ml in the unsuccessful group, the difference was not statistically significant ($p < 0.05$). Total protein concentration was found to be 6.67± 4.49 μ g/ml in the successful group and 33.55± 20.76 μ g/ml in the unsuccessful group ($p < 0.05$) thus it was higher in the successful group than the unsuccessful group (Table 2).

The success criteria of the treatment was determined as decreased pain on the postoperative 1st month compared to preoperative pain and the maximum mouth opening was ≥ 38 mm, the success rate of the arthrocentesis was 65.2% (15 cases) unsuccessful and 34.8% (8 cases) successful at postoperative 1st month (Figure 1).

4. Discussion

TMJ arthrocentesis is an effective treatment for TMD ID and is generally used for solving 3 main problems of TMD; limited mouth opening, pain and dysfunction [10,11,12]. Although it is widely used for different types of TMD, its mechanism is still not fully understood [13,14,15].

Besides, direct visualization of the TMJ was observed to be accompanied by inflammation of the ID, and this strengthened the role of proinflammatory cytokines in ID [4,16]. However, there are few reports on cytokines and cytokine receptors as a prognostic factor in arthrocentesis [15].

In the literature, Kanayama et al. found that the sIL-1RII concentration in synovial fluid was higher in the TMD group compared to healthy subjects in a study performed in 55 patients [5]. Although in our study, no comparison could be made because there was no healthy control group and performing arthrocentesis procedure to be performed in healthy patients was considered unethical. However, the relationship between sIL-1RII concentration amount and

treatment success was not statistically significant when the treatment was successful and unsuccessful. This may be since that all of the selected patients had CL, according to the studies, sIL-1RII was present in the synovial fluid of all TMD patients and also, proinflammatory cytokines could be affected not only by their receptors but also by other cytokines [5,6].

In this research, when the sIL-6R concentration was compared between the successful and unsuccessful groups, it was higher in the unsuccessful group was higher. Similarly, Kanayama et al [5] found that sIL-6R concentration was higher in patients with ID than the control group. Studies showed that IL-6 was found to be 89% in the synovial fluids of patients with ID, and a statistically significant relationship was found between IL-6 concentration and the severity of synovitis [17]. The higher amount of sIL-6R in the group considered to be unsuccessful in our study may be explained by the effect of this receptor on increasing the effects of IL-6 as stated in the literature.

The sTNF α -RI concentration in synovial fluid and its effect on the success of arthrocentesis procedure were examined between the successful and unsuccessful groups, there was no difference between these two groups in the present study. However Uhera et al. suggested that sTNF α -RI does not affect the level of disease and is not associated with maximum mouth opening and joint pain. Increase in this receptor concentration in synovial fluids in patients with severe deformity and disc displacement without reduction may be a sign of previous inflammation and degenerative processes [18]. Similar to this study, Kanayama et al. reported that sTNF α -RI concentration was higher in the TMD patient group compared to the control group [5]. In this study, the reason for obtaining this result might be considered as the diagnosis of all patients is TMD ID.

When the total protein concentrations in the synovial fluids between the successful and unsuccessful groups were compared, they were higher in the group in which the arthrocentesis procedure was considered to be unsuccessful, similar to the study by Kanayama et al. [5]. However, Nishimura et al. reported that the total protein concentrations were lower in the successful group compared to the unsuccessful group [10]. The reason for this may be explained by the fact that the total protein concentrations in synovial fluid are related to synovial inflammation based on the study by Kanayama et al. [5].

Since this study do not have a control group, it was not possible to fully evaluate the effect of treatment. because without the control group, it is unlikely to see whether the healing of symptoms is due to treatment or spontaneous recovery of the body. We can only suggest that proinflammatory cytokines in the synovial fluid may affect the success of the arthrocentesis.

5. Conclusion

As a result, especially due to agonist property of sIL-6R, and also the high protein concentrations in the synovial fluid, may be effective in treatment success, but sTNF α -RI and

sIL-RII concentrations in synovial fluid may not be effective in success of arthrocentesis. Having a better understanding of biochemical process that occur in TMJ synovial fluid will the diagnosis, management of TMJ and prognosis of treatment. Besides further studies are needed to determine the exact effect of these receptors on TMJ arthrocentesis.

6. Future Scope

The prognosis and success of TMJ arthrocentesis treatment cannot be predicted by the clinician. The effect of proinflammatory cytokines on this issue is still being discussed, whereas knowing the amount of specific cytokine receptors in the synovial fluid may be a predictor of treatment success. The limitation of this study was the low number of patients and the absence of a control group. A new vision can be created by working with more examples and control groups in the future

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