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## Evaluation of effectiveness of duloxetine in comparison to arthrocentesis in TMJ disorders

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### Abstract

**Aims:** The study was performed to evaluate the effectiveness of duloxetine in comparison to arthrocentesis in TMJ disorders.

**Materials and Methods:** The study comprised 45 patients with TMJ pain who were separated into three groups, each with 15 participants. Only TMJ arthrocentesis was given in Group A; only duloxetine therapy (30 mg) was given in Group B twice a day orally for three months; and a combination of TMJ arthrocentesis and duloxetine therapy (30 mg) was given twice a day orally for three months in Group C. Patients were tested in terms of pain, maximal mouth opening (mm), clicking, and estimation of interleukin 6 on the 1st day, 5th day, 7th day, 4th week, 6th week, and 12th week (IL 6).

**Results:** At weeks 4, 6, and 12, pain levels in Group C were much lower than in the other groups. On successive follow-ups, mouth opening in Group C grew much more than in Groups A and B. Postoperatively, biochemical examination of IL 6 levels in lavage fluid revealed a significant decrease in levels of IL 6 in Groups A and C.

**Conclusion:** According to the findings of this study, pain was significantly reduced following arthrocentesis combined with duloxetine medication. This combined therapy produces a considerably better and faster result, but it still necessitates long-term follow-ups with a larger number of patients.

**Keywords:** TMJ disorders, duloxetine, arthrocentesis

### 1. Introduction

The musculoskeletal disorder temporomandibular disorder (TMD) affects the masticatory system. Because of discomfort and locking in the temporomandibular joint, it has a severe influence on jaw function, causing patients to have limited mouth opening or difficulty chewing (TMJ) [1].

Displacement of the disc can present in a variety of ways, the most common of which are disc displacement with reduction (with or without intermittent locking) and disc displacement without reduction (with or without intermittent locking) (with or without limited opening). Pain, joint noises, and a deviated or uneven jaw function have all been linked to the disease.

The diagnosis should be based on the patient's medical history, clinical examination, standard and particular investigations, and radiographic evaluation. Because discomfort inhibits range of motion, which is required to maintain fluid flow in the joint for lubrication between the articular surfaces, TMJ-related problems must be managed [2].

Patients who do not react to conservative treatment are increasingly turning to arthrocentesis as a first-line surgical option. Arthrocentesis is supposed to break down joint adhesions and eliminate inflammatory mediators such as cytokines and interleukins (ILs) that cause chronic pain. When TMJ discomfort is relieved, mouth opening and functioning improve as well [3].

Duloxetine, a centrally active drug, has also been extensively researched and used in the treatment of pain associated with osteoarthritis of various joints. Duloxetine is a serotonin (5-HTP) and norepinephrine (NE) reuptake inhibitor that is selective and well-balanced. Chronic pain associated with central sensitization has been linked to an imbalance of 5 HT and NE. Duloxetine works by blocking the reuptake of serotonin and NE, which can reduce the synthesis of IL 6 and so relieve pain in these people [4,5].

In the present study, the purpose of the study is to investigate the effectiveness of duloxetine in comparison to arthrocentesis in TMJ disorders.

**Methodology**

The present study comprised forty five patients with TMJ disorder visiting the Outpatient Department of Oral and Maxillofacial Surgery. Diagnosis was made on the basis of history, clinical examination, and investigations. The treatment plan was thoroughly explained to each patient, and informed consent was taken. The ethical committee approval was obtained.

**Inclusion criteria**

1. Patients within the age limit between 18 and 60 years of age
2. TMJ pain of non-odontogenic origin as confirmed by the Research Diagnostic Criteria (RDC) for TMD/RDC axis II.
3. Pain on chewing or maximal mouth opening with a duration of at least 3 months.

**Exclusion criteria**

1. Patients having systemic autoimmune diseases
2. Patients having disturbed coagulation ability
3. Pain from traumatic injury.

The clinical assessment comprised TMJ examination. Routinely panoramic radiographic examination and cone-beam computed tomography of the joint were carried out for the all patients to rule out the dental cause of pain as well as to exclude TMJ abnormalities.

Patients who met inclusion criteria following screening were divided into three groups

**Group A:** 15 patients treated by TMJ arthrocentesis with Ringer’s lactate (approximately 200 ml) solution

**Group B:** Only duloxetine therapy (30 mg) given twice a day orally for 3 months

**Group C:** Combination of TMJ arthrocentesis with duloxetine therapy (30 mg) given twice a day orally for 3 months

Patients were followed at regular interval of the 1st day, 5th day, 7th day, 4th week, 6th week, and 12th week and assessed in terms of the following criteria:

1. **Pain:** Visual Analog Scale (0–10)
2. **Maximum mouth opening (mm):** Maximum interincisal distance
3. **Clicking:** Present/absent
4. Estimation of IL-6 was estimated in lavage fluid only in Group A and Group C by arthrocentesis on the first visit and postoperatively at 3 months. In Group B, only duloxetine therapy was given orally.

**Statistical analysis**

All the analysis was carried out on the SPSS 16.0 version by IBM (Chicago, IL, Inc., USA). The data were collected, compiled, and then analyzed using the Chi-square test. The one-way analysis of variance was used to compare normal discrete variables.  $P < 0.05$  was considered statistically significant.

**Results**

The present study involves 45 patients suffering from TMJ disorders. The pain was observed to be statistically non-significant between all the groups ( $P > 0.05$ ) preoperatively,

day 1, day 5, and day 7 after the treatment. The pain was found to be significantly different between the study groups ( $P < 0.05$ ) which was found to be lower in Group C than Group A and Group B at week 4, week 6, and week 12. [Table 1]

Preoperatively, the mouth opening was observed to be statistically non-significant ( $P = 0.07$ ) in all the groups. The mouth opening was observed to be significantly different in the study groups ( $P < 0.05$ ) which was found to be higher in Group C than Group A and Group B at day 1 and on subsequent follow-ups [Table 2]

There was no statistically significant ( $P > 0.05$ ) difference observed in clicking among the groups at all the time intervals preoperatively and postoperatively

There was no significant ( $P > 0.05$ ) difference in levels of IL-6 in lavage fluid between Group A and Group C by arthrocentesis on the first visit. However, a significant decrease was observed in levels of IL-6 in lavage fluid in Group A ( $P = 0.0001$ ) and Group C ( $P = 0.001$ ) postoperatively [Table 3].

**Table 1:** Comparison of pain at various interval in study groups

Time interval	Group A	Group B	Group C	P value
Pre operatively	5.31±1.22	5.52±1.25	6.02±1.09	0.44
Day 1	5.72±1.55	5.22±1.33	6.41±1.66	0.21
Day 5	4.81±1.36	5.22±1.29	3.91±1.77	0.18
Day 7	4.62±1.59	5.34±1.54	3.74±1.28	0.11
Week 4	3.50±1.53	4.58±1.33	2.70±1.24	0.04*
Week 6	3.50±1.67	4.09±1.42	2.21±1.54	0.03*
Week 12	3.30±1.09	5.00±1.87	1.71±1.87	0.001*

**Table 2:** Comparison of maximum mouth opening at various time intervals in study groups

Time interval	Group A	Group B	Group C	P value
Pre operatively	33.32±5.63	26.10±5.33	33.89±9.16	0.07
Day 1	32.71±6.88	26.10±4.40	34.01±9.88	0.04*
Day 5	34.00±7.17	26.11±4.42	37.30±9.86	0.006*
Day 7	34.61±7.00	26.21±6.87	38.91±9.67	0.003*
Week 4	36.29±6.57	26.90±4.32	40.01±8.66	0.001*
Week 6	36.77±6.44	27.10±4.40	41.07±7.73	0.001*
Week 12	36.50±6.65	26.46±3.86	40.91±7.55	0.001*

**Table 3:** Comparison of Lavage fluid

	Group A	Group B	Group C	P value
Pre operatively	12.60±7.55	-	9.34±5.99	0.52
Post operatively	5.86±1.55	-	5.01±1.16	0.44

**Discussion**

The aim of the study was to compare the efficacy of duloxetine therapy alone or in combination with TMJ arthrocentesis in the treatment of painful TMJ.

All patients enrolled in Groups A, B, and C had moderate-to-severe pain preoperatively. However, the reduction in pain was observed in all the groups postoperatively. Pain was found to be significantly reduced in Group C in comparison with Group A and Group B at week 4, week 6, and week 12. Pain in Group A was reduced more than Group B but the reduction of pain as highest in Group C supporting the combination therapy. [Table 1].

Dolwick and Nitzan <sup>[6]</sup>, revealed the similar results and supports the outcomes presented by the study. Our study results were found to be in accordance with the findings of the Emshoff *et al.* <sup>[7]</sup>, Sanromán <sup>[8]</sup>, Yura and Totsuka *et al.* <sup>[9]</sup>.

The mouth opening was observed to be comparable in all the groups preoperatively but was found to be significantly higher

in Group C than Group A and Group B on subsequent follow-ups [Table 2]. In group A, the mouth opening was found to be higher than group B.

Dolwick and Nitzan [6], in their study, found almost the similar results. This finding is in accordance with the findings of Dimitroulis *et al.* [3], Emshoff *et al.* [7], Sanromán [8], Yura and Totsuka *et al.* [9], in their studies that found almost the same results.

There was no significant difference in clicking postoperatively. Clicking was found to be reduced in patients of Group A as compared to Groups B and C. The results are in accordance with the outcomes observed by Carvajal and Laskin [10]. Thus, it was found that clicking was independent of either form of treatment or combination of them.

In Group A and Group C, the mean IL-6 levels measured in the lavage fluid were  $12.60 \pm 7.55$  pg/ml and  $9.34 \pm 5.99$  pg/ml pre operatively. After 3 months of treatment, the mean IL-6 values in Groups A and C were  $5.86 \pm 1.55$  pg/ml and  $5.01 \pm 1.16$  pg/ml, respectively. On postoperative evaluation, there was a significant decrease in IL-6 levels in both the groups ( $P = 0.0001$  and  $0.001$ ). There is no significant difference between Groups A and C in IL-6 levels in lavage fluid pre and post operatively. [Table 3].

IL 6 has been linked to acute synovitis, TMJ pain, and inflammation in TMJ fluid in several studies [11]. It has also been linked to increased T lymphocyte proliferation, B lymphocyte differentiation, and complement cascade activation [12]. In their investigation, Lee JK *et al.* [13] discovered that synovial levels of tumour necrosis factor (TNF) and interleukin 6 (IL 6) were raised in TMD patients with symptoms of acute pain, mouth opening limitation, and clicking. This is consistent with our findings, in which IL 6 levels were raised in all individuals with TMJ issues before to therapy. However, only Group A and Group C showed a reduction in these values after therapy. The findings of this study are similarly consistent with those of Nishimura *et al.* [14] who found a substantial difference in cytokines IL 1, IL 6, IL 8, IL 11, and TNF levels in patients following arthrocentesis, implying that the treatment procedure was effective. As a result, the amount of IL 6 in synovial fluid can be used as a prognostic indicator and may aid in the treatment of individuals with TMJ issues.

After 12 weeks of treatment, the content of IL 6 in lavage fluid in both groups (A and C) was found to be considerably lower in both groups (A and C). Patients in Group C experienced a considerable reduction in pain after receiving duloxetine. These findings are consistent with the findings of Zhao *et al.* [15], who found that after therapy with duloxetine, serum levels of IL 6, TNF, and IL 1 decreased significantly. This could be due to duloxetine's inhibitory effect on serotonin and NE reuptake, which results in less IL 6 production and thus less inflammation and discomfort.

As a result, the current study concludes that arthrocentesis relieves TMJ pain while also improving mouth opening and functioning. Rather than relocating the disc, it produces lysis and lavage in the superior joint area. It's also known to break down joint adhesions and eliminate inflammatory mediators like cytokines and ILs, which cause chronic pain.

## Conclusion

Arthrocentesis is becoming more widely acknowledged as the first-line surgical solution for individuals whose symptoms (pain and mouth opening) do not respond to conservative TMD therapy. In our research, pain was significantly reduced following arthrocentesis combined with duloxetine therapy

compared to arthrocentesis or duloxetine therapy alone. This combined therapy improves mouth opening significantly and quickly, although long-term follow-ups with a larger number of patients are still required.

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