

# COMPARISON OF THE EFFICACY OF TWO TECHNIQUES OF PROLOTHERAPY IN THE TREATMENT OF TEMPOROMANDIBULAR JOINT INTERNAL DERANGEMENT

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## ABSTRACT

**INTRODUCTION:** Internal temporomandibular joint (TMJ) derangements are uncomfortable conditions that result in mouth locking, malocclusion and joint dysfunction. Internal TMJ derangements can be treated with both minimally invasive and invasive methods.

**AIM:** The aim of this study is to compare the efficacy of two techniques of multiple points TMJ prolotherapy using dextrose versus liquid platelet rich fibrin in management of internal derangement of the temporomandibular joint.

**MATERIALS AND METHODS:** 30 patients were selected randomly and divided into two different groups. In group A injectable dextrose prolotherapy was used to treat individuals with internal derangements compared to injectable liquid platelet rich fibrin that was used in group B. The pain intensity, maximum mouth opening and jaw movement in the lateral and protrusion directions and joint noise, were recorded to compare between the outcome between both groups.

**RESULTS:** Pain level was significantly lowers in group B (I-PRF) at one week, one month, three months and six months intervals. ( $p \leq 0.05$ ) compared to group A. The maximum inter-incisal mouth opening is significantly higher in I-PRF group at one month, three months and six months than in group A. Statistically insignificant difference was reported regarding joint tenderness, range in jaw movement, and joint noise.

**CONCLUSION:** Considering the results of this study, it is possible to conclude that injectable platelet rich fibrin is more effective in terms of pain alleviation and improving mouth opening, while there is no noticeable difference in any other parameter between the two groups during the postoperative period.

**KEYWORDS:** Temporomandibular joint, internal derangement, prolotherapy, platelet-rich fibrin.

**RUNNING TITLE:** Efficacy of two prolotherapy techniques in treatment of internal derangement.

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## INTRODUCTION

People with TMJ conditions frequently notice a considerable decline in their quality of life due to destructive issues that affect their regular activities (1).

The temporomandibular joint is made up of the temporal bone, the jaw, several associated muscles, specialised fibrous tissue, the articular disc, and different ligaments (2).

Temporomandibular disorders, which are supposed to be one of the subcategories of musculoskeletal issues, were discovered to be a significant factor in the orofacial region's non-dental discomfort (3).

Among the most common forms of TMJ disorders is TMJ internal derangement, which 10% of people globally are affected, with young females having a higher prevalence (4).

The expression refers to an imbalance in the interaction of the articular eminence, condyle, and articular disc, which in turn affects joint stabilization and lubrication, blood circulation, waste removal,

and local administration of systemic medications (5, 6).

Splints are widely used by TMD patients to decrease aberrant muscle activity, heighten the vertical dimension, and improve TMJ stability. Despite being frequently utilized as the initial course of treatment, they are not always successful in treating TMD patients (7).

Different invasive and non-invasive treatment modalities are described for management of TMJD. Arthrocentesis is described as simple, unharmed and slightly invasive way for treatment of TMJD. Arthrocentesis demonstrates significant progress in reducing TMJ pain with opening and clicking of the mouth (8, 9).

In addition to arthrocentesis, steroids and sodium hyaluronate injections are two other frequent intra-articular injections (10).

Prolotherapy is an injectable therapy for regeneration that can be used profitably in joints of other body parts as knee problems and low back pain. Growth factors injections stimulate the outcome of

growth factors, which in turn improve growth of tissues and cells (11).

Prolotherapy is an uncomplicated, minimally invasive procedure that encourages the body's painful areas to heal by promoting the body's own natural healing process. Prolotherapy injection with dextrose induces better outcomes regarding limitation of pain and other TMD symptoms among patients suffering from internal derangement (12).

Platelet rich plasma is platelets concentration with related growth factors achieved by patient blood sample which is centrifuged after withdrawal. PRP has been introduced at first in the 1990's. PRP is considered to be a better supplement to TMJ internal derangement with effective assets involving antibacterial, anti-inflammatory and analgesic functions. In addition, it acts as a scaffold for differentiation and migration of cells restoring intra-articular HA functions, synthesis of glycosaminoglycans reaching joint balance angiogenesis (13).

Centrifugation at low speed was established as a way to develop the allocation and contents of cells with growth factors situated at the matrix of PRF (14).

Decreasing the relative centrifugation force with preservation of time to 8 mins liquid I-PRF is obtained with elevated collection of immune cells and growth factors in comparison with solid matrices of PRF (15).

As a result of lowering the centrifugation force with decreasing time of centrifugation to 3mins, additional growth factors were delivered, which increased the amount of inflammatory cells and platelets as a result, even at reduced relative centrifugation forces (16).

The severe TMJ internal derangement is furthermore confirmed besides the clinical diagnosis by magnetic resonance imaging (MRI) (17).

MRI is said to be the best method to determine the relation between TMJ disc and condyle other than any other techniques of imaging. Additionally, it is minimally invasive and there is no need for ionizing radiation for imaging (18).

The main objective of this study is to compare the efficacy of various types of prolotherapy (dextrose and liquid platelet rich fibrin) in management of internal derangement of the temporomandibular joint

## PATIENTS AND METHODS

### Study design

This study used a 1:1 allocation ratio in a randomized clinical trial. It was organized and reported in accordance with the CONSORT guidelines.

The predicted sample size was based on a 5% alpha error and an 80% research power. 14 patients per group was the minimal sample size, which was expanded to 15 patients to account for cases that were

lost to follow-up. Total sample size = Number per group x Number of groups = 15 x 2 = 30 patients. This study was performed on 30 patients. The patients were picked from the Alexandria University Teaching Hospital's outpatient clinic and operated on in the Oral and Maxillofacial Surgery Department, Faculty of Dentistry, Alexandria University.

Thirty patients were randomly allocated and separated into two groups. In group A patients with internal derangement were treated with injectable dextrose prolotherapy in comparison with injectable liquid platelet rich fibrin that was used in group B. Both surgeon and data analysts were blinded to the treatments.

In order to assure and verify their awareness of the procedure's potential outcomes and the risks involved, every patient signed an informed consent form prior to the procedure.

The clinical portion of the study was carried out following clearance from the Faculty of Dentistry, Alexandria University's Research Ethics Committee.

### Inclusion criteria

Patients with internal derangement examined clinically based on mandibular range of motion assessment, inter-incisal opening and joint tenderness when palpated, present or absent and confirmed with MRI diagnosis.

Patients with TMJ discomfort; particularly when opening, joint noises, limitation in mouth opening, restricted lateral motion in the direction of the unaffected side.

Deviation in opening and protrusion movements to the injured side.

All patients were shown to be resistant to conservative therapy. Prior to enrolling the participants in the trial, appropriate nonsurgical methods were used to treat them. NSAIDs, a soft diet, moist heat, and behaviour modification (occlusal splints) were some of these treatment options.

### Exclusion criteria included

Patients with any systemic illnesses or abnormalities of platelet function, patients who have had TMJ surgery in the past, patients who have had an infection or joint fracture previously.

Patients receiving NSAIDs or anticoagulant therapy within 48 hours before surgery, as well as systemic or local corticosteroid use.

Autoimmune conditions, significant mechanical mouth opening obstructions, benign or neoplastic TMJ lesions.

### Materials

Centrifugal machine for PRF preparation (Wotefusi 80-1 electric centrifuge, china)

Ready-made pure Dextrose (Otsuka Ateco pharma Egypt)

5 ml syringe. (Masco, Egypt)

PRF C-tubes (Houdior, China)

### Methods

### Clinical examination

Evaluation of mandibular range of motion (ROM): The maximum inter-incisal opening was calculated as the vertical distance, in millimetres, between the upper and lower central incisors at the maximal pain-free mouth opening, painful opening and assisted maximum opening.

The range of lateral and protrusive motions of the mandible was measured as the horizontal distance, measured in millimetres, between the upper and lower midlines.

Observation of deviation on mouth opening.

Joint tenderness on palpation was noted as present or absent as tender or not tender.

When moving the jaw, a mild bilateral digital TMJ palpation was used to determine whether joint noises were present or absent.

### Radiographic Examination

Panoramic radiographs were taken to exclude dental cause of pain. MRI was used to see the stage of displacement to confirm the clinical diagnosis.

### Operative phase

Magnetic resonance imaging (MRI) confirmed internal TMJ dysfunction in all individuals (Figure 1). Both groups received occlusal splints for a period of two weeks.

### Technique

For patients of study group A (dextrose prolotherapy). Ready-made, 50% pure dextrose solution was drawn into a 5 ml syringe and combined before being injected using a 22-gauge needle to create the prolotherapy solution. The patient was draped, painted, and in a semi-supine position.

Using infiltration anaesthesia, three target areas received injections of the prolotherapy solution:

Posterior joint space. A line was drawn from the canthus of the eye to the tragus of the ear; there was a depression that appeared after opening the jaw widely prior to the tragus of the ear served as a clear indication of this site. One ml of injectable prolotherapy solution was applied here (Figure 2).

Anterior disc attachment to the lateral pterygoid muscle. While closing the mouth after opening the jaw widely; this was noticed by the depression adjacent to the condyle anterior the tragus of the ear. One ml of the injectable solution was applied (Figure 3).

Masseter attachment. Palpable masseter muscle was detected. The injectable solution was administered with 1 ml into the site that was found to be the most tender (Figure 4).

Prolotherapy injections were given as follows: First one given on the first day; second injection given four weeks later.

For patients of group B (injected liquid PRF)

### Liquid platelet-rich fibrin preparation

Using sterile, uncoated plastic tubes without additives, an aseptic technique was used to obtain blood from the

antecubital vein, which was then immediately centrifuged. To obtain liquid PRF, a low speed centrifugation procedure of (700 rpm) for 3 minutes was applied (15).

The liquid PRF was at the top of the tube, and red blood cells were at the bottom, with a ratio of roughly 7:2. These layers were separated following centrifugation. Three mL syringe was used to aspirate liquid PRF. (Figure 5).

### Injection technique

Points of injections were determined & marked & anesthesia (3% Mepecaine) was administered by infiltration in the target areas prior to the injection of liquid PRF.

The same oral and maxillofacial surgeon performed all injections. Antiseptic solution was used to clean the preauricular region's skin surface, and the same three specific sites as previously demonstrated with dextrose solution were injected with liquid PRF.

### Postoperative care

Patients were instructed to follow a soft diet and taking paracetamol (500 mg) twice daily for two days after the injection are recommended. TMJ discomfort was assessed using a visual analogue scale (VAS I), with 0 signifying no pain and 10 denoting extreme pain. Using a millimetre scale, mouth expansion (interincisal distance) and deviation were measured. Joint auscultation was used to record joint noises (clicking). Joint noises were indicated by a score of 1, and joint sounds were absent by a score of 0. Preoperatively and postoperatively at one, three and six months, these parameters were evaluated.

### Statistical analysis of the data

The IBM SPSS software package version 20.0 was used to analyse the data after it was entered into the computer. (Armonk, NY: IBM Corp)

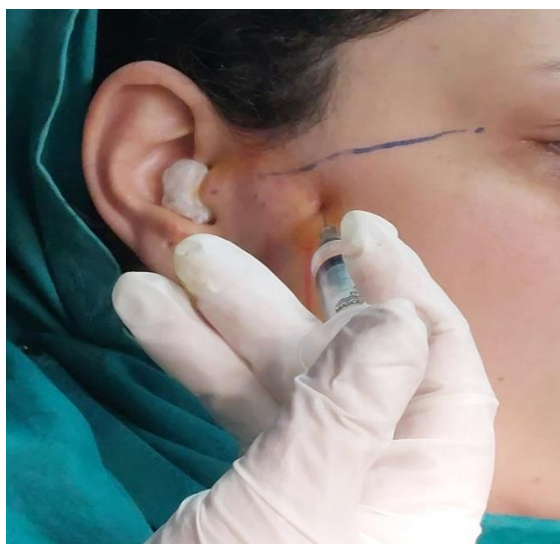
Numbers and percentages were used to describe qualitative data. The normality of the distribution was checked using the Smirnov test. The range (minimum and maximum), mean, standard deviation, median, and interquartile range were used to characterise quantitative data (IQR). The 5% level of significance was utilized to evaluate the significance of the data.



Figure 1: MRI diagnosis.



**Figure 2:** Injection into posterior joint space.



**Figure 3:** Injection into anterior disc attachment.



**Figure 4:** Injection into the most tender area of the masseter.



**Figure 5:** I- PRF.

### RESULTS

Based on inclusion criteria, thirty patients were admitted to the faculty of dentistry at Alexandria University's oral and maxillofacial surgery department. Patients were split up into two groups, each with fifteen patients. Group (A) was treated dextrose prolotherapy, while group (B) was treated with injectable liquid PRF. The included population sample showed a significantly higher percentage of females (86.7%) in comparison to males (13.3%)

In group A, the mean recorded preoperative pain intensity was  $8.47 \pm 0.64$  after 1 week was  $5.27 \pm 1.03$ , after 1 month was  $3.60 \pm 1.12$ , after 3 months was  $2.53 \pm 1.06$  and after 6 months was  $3.07 \pm 1.16$  while in group B the mean recorded preoperative pain intensity was  $8.20 \pm 0.94$  after 1 week was  $2.80 \pm 1.32$ , after 1 month was  $2.40 \pm 1.24$ , after 3 months was  $1.87 \pm 0.52$  and after 6 months was  $1.73 \pm 0.96$  (table 1, figure 6).

Pain level was significantly lower in group B (I-PRF) at one week, one month, three months and six months intervals ( $p \leq 0.05$ ).

The maximum inter-incisal mouth opening showed statistically insignificant differences between group A and group B in the preoperative and 1 week intervals while it is significantly higher in I-PRF group at one month, three months and six months ( $p \leq 0.05$ ) (Table 2, Figure 7).

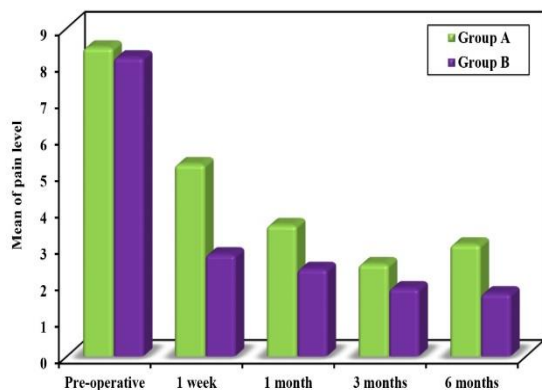
The comparison regarding the joint tenderness, Protrusive and lateral movements and joint clicking showed statistically insignificant differences between group A and group B were preoperatively twelve patients of group A had clicking, at 1 week five patients had clicking, at 1 month eight patients had clicking, at 3 months eight patients had clicking and at 6 months' nine patients had clicking.

In group B preoperatively twelve patients had detectable joint sounds, at 1 week four patients had clicking, at 1 month eight patients had joint clicking, at 3 months eight patients had clicking and at 6 months' nine patients had joint sounds.

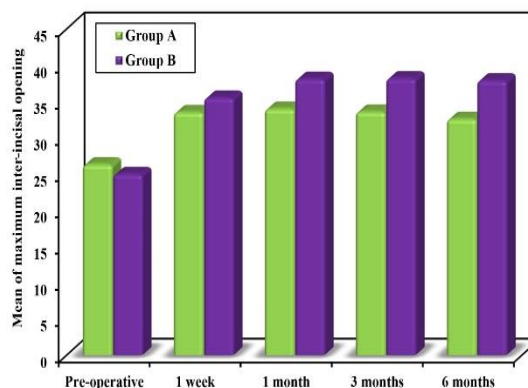
In group A the mean preoperative value of the jaw movement toward the contra-lateral unaffected side was  $3.07 \pm 1.22$ , after 1 week was

4.67 ± 0.98, after 1 month was 4.93 ± 0.88, after 3 months was 4.53 ± 0.99 and after 6 months was 4.40 ± 0.99.

In group B the mean preoperative value of the jaw movement toward the contra-lateral unaffected side was 2.13 ± 1.19, after 1 week was 4.47 ± 0.99, after 1 month was 5.20 ± 0.77, after 3 months was 5.0 ± 0.93 and after 6 months was 4.93 ± 0.96.



**Figure 6:** Comparison between the two studied groups according to pain level.



**Figure 7:** Comparison between the two studied groups according to maximum inter-incisal opening.

**Table (1):** Comparison between the two studied groups according to pain level.

Pain level	Group A (n = 15)	Group B (n = 15)	t	P
Pre-operative				
Min. – Max.	7.0 – 9.0	6.0 – 9.0		
Mean ± SD.	8.47 ± 0.64	8.20 ± 0.94	0.907	0.372
Median (IQR)	9.0 (8.0 – 9.0)	8.0 (8.0 – 9.0)		
1 week				
Min. – Max.	4.0 – 7.0	0.0 – 5.0		
Mean ± SD.	5.27 ± 1.03	2.80 ± 1.32	5.700*	<0.001*
Median (IQR)	5.0 (4.5 – 6.0)	3.0 (2.0 – 4.0)		
1 month				
Min. – Max.	2.0 – 6.0	0.0 – 4.0		
Mean ± SD.	3.60 ± 1.12	2.40 ± 1.24	2.777*	0.010*
Median (IQR)	3.0 (3.0 – 4.0)	3.0 (1.5 – 3.0)		
3 months				
Min. – Max.	1.0 – 4.0	1.0 – 3.0		
Mean ± SD.	2.53 ± 1.06	1.87 ± 0.52	2.190*	0.040*
Median (IQR)	3.0 (2.0 – 3.0)	2.0 (2.0 – 2.0)		
6 months				
Min. – Max.	1.0 – 4.0	0.0 – 4.0		
Mean ± SD.	3.07 ± 1.16	1.73 ± 0.96	3.423*	0.002*
Median (IQR)	4.0 (2.0 – 4.0)	2.0 (1.0 – 2.0)		

**Table (2):** Comparison between the two studied groups according to maximum inter-incisal opening.

Maximum inter-incisal opening	Group A (n = 15)	Group B (n = 15)	t	P
Pre-operative Min. – Max. Mean ± SD. Median (IQR)	19.0 – 33.0 26.33 ± 4.62 25.0 (22.5 – 30.0)	19.0 – 35.0 25.0 ± 5.45 23.0 (20.5 – 29.0)	0.722	0.476
1 week Min. – Max. Mean ± SD. Median (IQR)	27.0 – 40.0 33.53 ± 3.96 35.0 (31.0 – 36.5)	29.0 – 42.0 35.53 ± 4.37 36.0 (32.0 – 39.0)	1.313	0.200
1 month Min. – Max. Mean ± SD. Median (IQR)	29.0 – 39.0 34.0 ± 3.14 35.0 (31.5 – 36.0)	32.0 – 43.0 38.13 ± 3.93 40.0 (34.5 – 41.5)	3.185*	0.004*
3 months Min. – Max. Mean ± SD. Median (IQR)	28.0 – 40.0 33.60 ± 3.50 33.0 (31.0 – 35.5)	30.0 – 43.0 38.20 ± 3.99 38.0 (35.0 – 41.5)	3.358*	0.002*
6 months Min. – Max. Mean ± SD. Median (IQR)	26.0 – 39.0 32.60 ± 3.89 32.0 (30.0 – 35.5)	30.0 – 43.0 37.93 ± 3.67 38.0 (35.0 – 40.5)	3.862*	0.001*

## DISCUSSION

Temporomandibular joint disorders are variety of poorly controlled problems that cause jaw pain and make it difficult to carry out daily activities like chewing and swallowing. TMD arises when the jaw's muscles and joints don't cooperate with one another. When pain increases, it would lead to impairment of function and limitation of mouth opening. Hence, correction of one problem can accelerate the improvement of the other (19, 20).

Dolwick et al. define internal derangement of TMJ as disturbance in the internal functioning of the TMJ, in particular the disc that is dislocated from its attachment to the mandibular condyle. This may occur due to macro or micro trauma, Para functional habits, occlusal malformation and emotional stresses (21).

Mejersjö C, Hollender L. assumed that radiographic examination is mandatory to assess differential diagnosis and to eliminate other forms of pathological conditions among painful TMD (22). In this study patients have been picked up complaining from signs and symptoms of internal derangement. Thirty have been selected, twenty-six patients were females and four patients were males. This coincides with the study by Gesch D et al. Who have assumed that females showed to be at a higher risk to develop TMD pain (23).

Nitzan et al. have reported that arthrocentesis is a minimally invasive simple method of internal derangement treatment that involves cleaning out debris (24).

Vankdoth S. et al. have defined prolotherapy as a regeneration injectable therapy that promoted cell proliferation by causing the migration of macrophages, monocytes, and granulocytes to the site in order to restore the joint structures. These inflammatory mediators promote growth factor releasing and fibroblast activation, which results in the production of new collagen fibres (25).

The main goal of this study is to compare between the efficacy of two techniques of prolotherapy in the treatment of internal derangement in which dextrose prolotherapy is performed in the present study under infiltration anesthesia for group A while injectable I-PRF was performed to group B.

Shaffer et al. have suggested that dextrose prolotherapy can be utilized to treat intradiscal, peridiscal, and muscle spasms alone, or with sterile water, or coupled with lidocaine, in addition, when applied to painful muscular trigger points or terminal muscle attachments, it produces excellent benefits. (26).

Rabago et al. have reported that the most popular Prolotherapy treatment solution is hypertonic dextrose that shows good results in many clinical trials (27).

Refai et al. also reported that multiple injections of dextrose prolotherapy have been shown promising outcomes, which in turn agrees with our study that shows significant increase in maximal mouth opening and range of mandibular movements(28). Moreover, Hakala and Ledermann

also have shown that multiple dextrose injections give significant therapeutic effects (29).

Carvajal and Laskin have reported that the reduction in pain intensity lead to improvement in maximal mouth opening, which sequentially causes decreasing in TMJ dysfunction. Hence, the improvement of one issue can speed up the resolution of another which agrees with the findings of the present study where there is opposite relation between pain level and other parameters of jaw movements where the reduction in pain intensity lead to improvements in maximal mouth opening, the mandible's degree of lateral and protrusive motion (19).

The present study's findings demonstrated a considerable expansion of mandibular motions, including lateral, protrusive, and maximal mouth opening, following prolotherapy which agrees with Priyadarshini et al. in a study of 34 patients who concluded that dextrose prolotherapy leads to improvement of mouth opening and decreasing in pain intensity (30).

In a study of 14 patients ELwerfelli et al. have reported that injection with 50% dextrose following arthrocentesis showed better effects in all parameters including pain intensity, range of mandibular motion and joint tenderness than arthrocentesis alone, which in turn agrees with our study that shows significant increase in maximal mouth opening and range of mandibular movements (31).

The goal of regenerative therapy is to rehabilitate normal structure and function beyond symptomatic relief. New therapeutic treatment protocols have been tested for treatment of painful TMJ internal derangement consists of intra-articular liquid PRF injection every two weeks. The patient continued to report advancement in a shorter interval of time compared to what reported by authors using PRP work towards the beneficial physiological effects from the standard blood concentrated injections (32-34).

Knezevic et al. have reported that PRP has the ability to comfort pain through the effect of growth factors that helps in tissue regeneration. They also assumed that PRP may be the future of management of pain. This agrees with our study, where it shows significant decrease in pain intensity where pain level was significantly lower in group B (I-PRF) at one week, one month, three months and six months intervals (35).

Cömert Kiliç et al., have evaluated the improvement of internal derangement signs with PRP injection. They have reported a statistically significant improvement in all of the parameters across the follow up period (36). This agrees with our study results revealing the considerable effect of platelet concentrates on improvement of patient suffering.

J.B. Albilal in a study of 48 patients complaining of TMJ disorders where 37 patients had painful internal derangement, stated that 33 out of the 48 patients showed significant reduction of pain when injected with liquid I-PRF at 8 weeks, 6 and 12 months while 15 of 48 are non-responders (15). This, in turn, agrees with our study as pain level was significantly decreased along the different periods of one week, one month, three and six months. In the same study, they have reported that the increase in mouth opening was statistically insignificant. This was in contrast to our study, where patients in group B have shown significant increase in maximum mouth opening compared to group A especially in the intervals of one month, three months and six months follow-up.

In a study of 36 patients U. Karadayi and B. Gursoytrak have stated that PRF when injected after arthrocentesis showed better results than arthrocentesis alone. In addition, it should be superior to use PRF in severe cases dysfunction which agrees with our study as group B showed better outcome in terms of pain level and mouth opening (37).

Ghoneim et al. have reported in a study that there was statistically significant difference in pain level, clicking and improvement in mouth opening between I-PRF group compared to arthrocentesis group which agrees with our study in terms of pain level and maximum mouth opening but in contrast in terms of clicking as there was no significant difference between group A and B according to clicking (38).

The present study's findings demonstrated that the level of pain significantly decreased and an improvement in maximal mouth opening that is significant in I-PRF group was detected when compared with dextrose group. This result is in accordance with Yuce and Komerik who reported that there was significant improvement in pain level and maximum mouth opening in the arthrocentesis plus i-PRF group compared to arthrocentesis alone or with HA at nine and 12 months follow-up (39).

Moreover, in a study of 54 patients Torul D, et al. have reported that PRF after arthrocentesis has better results than arthrocentesis alone in terms of pain intensity and mouth opening or with HA which agrees with our study as group B showed better outcome in terms of pain level and maximal mouth opening (40).

## CONCLUSION

Based on the findings of our research, we determine that injectable platelet rich fibrin was found to be superior in terms of reduction of pain and improving inter-incisal opening, while there are no significant differences between the two groups in other parameters throughout the postoperative period.

## CONFLICT OF INTEREST

The authors declare no conflicts of interest.

## FUNDING

No specific funding was received for this work.

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