

Clinical Evaluation Comparing The Effect Of Intra-Articular Injections Of Platelet Rich Plasma Versus Injectable Platelet Rich Fibrin In Conjunction With Arthrocentesis In Management Of Temporomandibular Joint Osteoarthritis

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ARTICLE INFO.

Keywords:

Temporomandibular joint,
Arthrocentesis, Injectable
platelet-rich fibrin,
osteoarthritis, platelet-rich
plasma

Abstract

Background: One of the most significant temporomandibular joint disorders (TMD) is temporomandibular joint osteoarthritis (TMJ-OA). A variety of treatment modalities were proposed to achieve pain relief & restore normal function of the temporomandibular joint in patients. Hence, the purpose of this research was to clinically evaluate the efficacy of intra-articular (PRP) injections in combination with arthrocentesis compared to (i-PRF) injections in combination with arthrocentesis in management of patients with (TMJ OA).

Methods: 45 eligible patients with (TMJ-OA) were selected from the outpatient clinic of the Oral and Maxillofacial Surgery Department, October University for modern sciences and arts, Cairo, Egypt. Patients were randomly assigned one of the three treatment groups: Group I: patients treated with arthrocentesis alone (control group) Group II: patients treated with a combination of arthrocentesis and intra-articular (PRP) injection Group III: patients treated with a combination of arthrocentesis and intra-articular (i-PRF) injection The three groups were compared to each other regarding the improvement in pain using visual analogue scale (VAS) & maximum mouth opening (MMO).

Results: Comparing the three groups to each other's the VAS scores variation between them was statistically non-significant ($p > 0.05$) preoperatively, while at one month, three months and six months postoperatively there was a significant decrease ($P \leq 0.05$) at the VAS scores with best results for group III followed by group II in comparison with control group I. When the three study groups were compared to each other's the Maximum Mouth Opening (MMO) scores variation between them was statistically non-significant ($p > 0.05$) preoperatively, while at one month, three months and six months postoperatively there was a significant increase ($P \leq 0.05$) at the MMO scores with best results for group III followed by group II in comparison with control group I.

Conclusion: Intraarticular injection of i-PRF following arthrocentesis is a successful treatment with better comparable reported results than intraarticular injection of PRP following arthrocentesis in management of TMJ OA.

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1 Introduction

One of the most significant temporomandibular joint disorders (TMD) is temporomandibular joint osteoarthritis (TMJ-OA). The reported prevalence of osteoarthritis differs broadly from 8% to 76% in different populations with the usual age group of presentation in the third to fifth decades of life.¹⁻⁴ The main clinical manifestations of (TMJ-OA) include pain, abnormal joint sounds, and limited joint activity.^{5, 6} A variety of treatment

modalities were proposed to achieve pain relief and restore normal function of the temporomandibular joint in patients suffering from TMD, with nonsurgical methods preferred as initial treatment options.⁷⁻⁹ The mechanical and biological characteristics of TMJ structures are intended to be enhanced by these therapeutic approaches.^{1,10} One of the least invasive ways to treat (TMJ-OA) is using arthrocentesis and intraarticular injections.¹¹

Arthrocentesis was found to be the least invasive & simplest technique in the management of (TMJ-OA). This method aims to remove inflammatory mediators & reduce pressure inside the joint.^{2,12,13} It showed highly effective results in the reduction of pain & the regeneration of the normal range of TMJ motion in patients with (TMJ-OA).^{10,14} However, the efficiency of arthrocentesis alone was temporary & did not play a role in the rehabilitation of the microarchitecture of the TMJ.

Platelet-rich plasma (PRP) is a preparation of plasma with a high concentration of platelets, which release growth factors that help in tissue healing. Therefore, the administration of (PRP) has lately gained admiration in the treatment of (TMJ-OA) owing to its palliative & anti-inflammatory properties.^{9, 15-17} Recent studies showed that (PRP) injection significantly improved pain & mouth opening in patients suffering from (TMJ-OA) with superior results than that of arthrocentesis alone.^{8,9,15}

Unfortunately, (PRP) preparation necessitates the addition of anti-coagulants that results in suppression of wound healing process despite of the regeneration achieved from growth factors released. As a result, a second generation of platelet concentrates known as platelet-rich fibrin (PRF) was created.¹⁸

The innovation of low speed centrifugation method produced injectable PRF (i-PRF) which is a liquid form of PRF. This formula of PRF stays in liquid state for several minutes after centrifugation, allowing its injection. This preparation of platelet concentrate facilitated the release of growth factors providing a better environment for tissue repair & regeneration.^{19,20} However, intraarticular injection (i-PRF) in conjunction with arthrocentesis has been evaluated in few studies with limited publications on its effectiveness in patients with (TMJ-OA).²¹⁻²⁶ To our knowledge, no study has compared the effectiveness of

PRP and i-PRF injections in conjunction with arthrocentesis for the treatment of TMJ-OA.

Hence, the purpose of this research was to assess the clinical effectiveness of intra-articular (PRP) injections in combination with arthrocentesis compared to (i-PRF) injections in combination with arthrocentesis in the management of patients with (TMJ OA).

2 Methods

2.1 Sample size:

Based on the previous study by Gözde Işık et al.²⁶ regarding the differences in pain scores across the study groups, the sample size for this investigation was determined to be 15 patients per group, with a 95% statistical power and a significance level of 0.05. The G*Power program (University of Düsseldorf, Düsseldorf, Germany) was used to calculate the sample size.

2.2 Patient selection and study design:

Patients selected from the outpatient clinic of the Oral and Maxillofacial Surgery Department, October University for Modern Sciences and Arts, Cairo, Egypt.

The current study achieved the approval of the ethical committee of MSA University No: 3102 following the Declaration of Helsinki on medical protocol & ethics. Patients included in the study were educated about the nature of the study as well as the risks & benefits of the procedure & signed written informed consents for the treatment plan.

Inclusion Criteria:

- Patients with osteoarthritis (OA) of one or two temporomandibular joint (TMJ)
- limited mouth opening
- localized pain of the affected joint

Exclusion Criteria:

- Systemic or malignant diseases affecting TMJ-OA assessment
- Previous invasive or surgical treatments of TMJ unrelated to OA
- Edentulous patients
- Pregnancy

2.3 Patients grouping:

The patients with (TMJ-OA) were randomly assigned to one of the three treatment groups:

Group I: patients treated with arthrocentesis alone (control group)

Group II: patients treated with a combination of arthrocentesis and intra-articular (PRP) injection

Group III: patients treated with a combination of arthrocentesis and intra-articular (i-PRF) injection

2.4 Study outcomes:

- **Primary outcome variable:** Pain will be assessed using the visual analogue scale (VAS). Rated from zero = no pain to ten = worst pain.

- **Secondary outcome variable:** change of maximum mouth opening (MMO) measured as the distance between the incisal edge of the upper and lower central incisors

The three groups were compared to each other regarding the improvement in pain value & maximum mouth opening.

2.5 Pre-Operative Phase:

All personal information, including comprehensive medical and dental histories, was documented for every patient. To assess clinical factors, a comprehensive clinical examination was carried out. The VAS was used to assess pain, with Zero score for no pain & ten score for worst pain experienced.²⁷ The maximum unassisted mouth opening was measured in millimetres (mm) using a Vernier calliper. (Fig.1) Measurements were first taken preoperatively (baseline) and then repeated at one month, three months and six months postoperatively.



Figure 1. Measurement of maximum unassisted mouth opening

Magnetic Resonance Imaging:

All patient were evaluated radiographically using Magnetic resonance imaging (MRI) (open and closed) to confirm the diagnosis of osteoarthritis (OA) of temporomandibular joint (TMJ) (Fig.2: a, b)

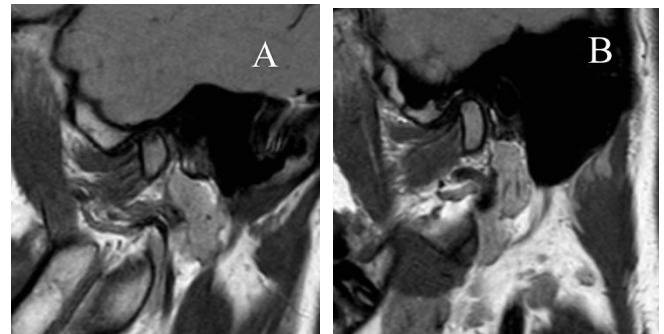


Figure 2. Magnetic resonance imaging (MRI) for TMJ-OA confirmation of diagnosis.

2.6 Operative Phase:

The procedure was performed under local anesthesia using Mepecaine- L (Mepevacaine Hcl 2% with Levonordefrin 1:20,000, Alexandria Co. For Pharmaceuticals, Alexandria, Egypt). After adequate preparation of the surgical field with an antiseptic solution, the auriculotemporal nerve was approached at a point 10 mm anterior to the ear tragus & 2 mm below the canthus-tragus line.¹² About 1 ml of the local anaesthetic agent is then injected while the patient is instructed to widely open his/her mouth.

Group I: Arthrocentesis alone (control group)

Arthrocentesis procedure

Arthrocentesis was performed using the standard two-needle technique proposed by *Nitzan et al.*¹² The canthus-tragus line was used for anatomical orientation. Two guiding points were marked over the skin. The posterior point is located along the canthus-tragus line 10mm from mid-tragus & 2 mm below this point matching the glenoid fossa. The anterior point is 20 mm in front of the tragus along the canthus-tragus line & 10mm below it representing the articular eminence. The patient was instructed to open his/her mouth widely while the mandible in protruded position. Then a 20-gauge needle was inserted at the first point & 2 ml of lactated Ringer solution was injected into the superior joint space. This is followed by insertion of a second needle of the same gauge at the second marked point. Joint space lavage was performed with 100 ml of 5% lactate solution with the inflow through the first needle and the outflow through the second needle. For *Group I* (the control group) treatment was considered completed and the two needles were removed gently. (Fig.3)



Figure 3. Arthrocentesis procedure.

Group II: Arthrocentesis followed by intra-articular (PRP) injection

Preparation of Platelet-Rich Plasma (PRP)

PRP was prepared using a single-step centrifugation procedure as described by *Anitua*.²⁸ For PRP preparation venous blood was collected from the patient & drawn into glass test tubes containing sodium citrate as an anticoagulant. The collected blood was mixed with the anticoagulant by rotating movement and then centrifuged at 1,000 rpm for ten minutes at room temperature. After centrifugation three distinctive layers were obtained: the yellow top layer containing platelet-poor plasma (PPP), the middle buffy coat layer containing (PRP) & the bottom red layer of red blood cells. The PRP was carefully collected into separate syringe. (Fig.4)

For patients in *Group II* after the arthrocentesis procedure was completed the second needle was removed and PRP was injected through the first needle into the superior joint space. About 1 to 1.5 ml of PRP was injected and the mandible was gently manipulated. (Fig.5)



Figure 4. PRP preparation



Figure 5. PRP injection into superior TMJ space following arthrocentesis.

Group III: Arthrocentesis followed by intra-articular (i-PRF) injection

Preparation of injectable platelet rich fibrin (i-PRF)

For the preparation of (i-PRF), the technique described by *Choukroun et al.*²⁹ was followed. About 10 ml of venous blood was collected from the patient & drawn into sterile uncoated tubes. Blood was immediately centrifuged at 700 rpm for three minutes. After centrifugation, two distinctive layers were obtained: the upper layer containing (i-PRF) & the layer of red blood cells. i-PRF was then collected into separate syringe. (Fig.6)

For patients in *Group III* following the arthrocentesis procedure, the second needle was removed & about 1 to 1.5 ml of i-PRF was injected into the superior joint space through the first needle and the mandible was gently manipulated. (Fig.7)



Figure 6. i-PRF preparation



Figure 7. i-PRF injection into superior TMJ space following arthrocentesis.

2.7 Post-operative phase:

Patients were instructed to apply moist heat & use a soft diet postoperatively along with suitable jaw exercises. Analgesics (Catafast 50mg; each tablet contains 50mg of Diclofenac potassium. Novartis Pharmaceuticals, Cairo, Egypt) were prescribed to control postoperative

pain as well as suitable antibiotics (Augmentin: each tablet containing 875 mg amoxicillin as amoxicillin trihydrate & 125 mg clavulanic acid as potassium clavulanate, Medical Union Pharmaceuticals (MUP), Cairo, Egypt) for one week to minimize the risk of TMJ infection.

2.8 Post-Operative Follow-Up:

Patients were recalled at regular intervals of one month, three months and six months postoperatively for assessment of pain & maximum mouth opening.

2.9 Statistical analysis:

Collected data were statistically analyzed using SPSS ver. 22 software (statistical package for social science on Windows 2013) with a probability value of $p \leq 0.05$. Changes in preoperative and postoperative data regarding VAS & MMO in the same group were evaluated using the Student T test (paired) to assess the significance of the difference. The groups were then compared to each other similarly using ANOVA test (Analysis of Variance). Comparing every two groups was conducted using the Post Hoc correction test.

3 Results

The present study involved 45 eligible patients (15 males & 30 females) with TMJ-OA, Patients mean age was 33.5 years.

The current study was conducted to evaluate the efficacy of intra-articular (PRP) injections in combination with arthrocentesis compared to (i-PRF) injections in combination with arthrocentesis, the two groups were also compared to the control group of arthrocentesis only in management of patients with (TMJ OA). All patients were assessed clinically before and after intraarticular injections. Neither clinical side effects nor complications were reported. All patients showed uneventful healing throughout the study intervals.

Group I (control group):

VAS scores:

The Mean VAS score was (8.07 ± 0.80) preoperatively, decreased significantly ($p \leq 0.05$) at one month (4.87 ± 0.74), three months (4.53 ± 0.64), and six months (4.87 ± 0.64) postoperatively. Although there

was a significant decrease ($p \leq 0.05$) in the VAS scores through all intervals, yet a non-significant decrease ($p \geq 0.05$) was found comparing the one-month with the six months follow-up periods. **Table 1**

Table 1. Showing means of VAS of the Study group I

Pain scores (VAS) Control (group I)				
	Before	1month	3 month	6 month
Mean	8.07	4.87	4.53	4.87
SD	0.80	0.74	0.64	0.64
Min	7	4	4	4
Max	9	6	6	6
1 month	<u>0.000</u>			
3 month	<u>0.000</u>	<u>0.019</u>		
6 month	<u>0.000</u>	<u>1.000</u>	<u>0.019</u>	

Maximum Mouth Opening (MMO):

The Mean MMO score was (30.11 ± 0.69) preoperatively, increased significantly ($p \leq 0.05$) at one month (35.07 ± 0.62), three months (35.45 ± 0.58) and six months (35.49 ± 0.47) postoperatively. Although there was a significant increase ($p \leq 0.05$) in the MMO scores through all intervals, yet a non-significant increase ($p \geq 0.05$) was found comparing the three-month with the six-month follow-up periods. **Table 2**

Table 2. Showing means of MMO of the Study group I

MMO Control group (group I)				
	Before	1month	3 month	6 month
Mean	30.11	35.07	35.45	35.49
SD	0.69	0.62	0.58	0.47
Min	28.7	34	34.4	34.9
Max	31	36	36.1	36.1
1 month	<u>0.000</u>			
3 months	<u>0.000</u>	<u>0.000</u>		
6 months	<u>0.000</u>	<u>0.006</u>	<u>0.756</u>	

Group II (PRP group):**VAS scores:**

The Mean VAS score was (8.13 ± 0.83) preoperatively, decreased significantly ($p \leq 0.05$) at one month (3.87 ± 0.74), three months (3.40 ± 0.63), and six months (3.47 ± 0.74) postoperatively. Although there was a significant decrease ($p \leq 0.05$) in the VAS scores through all intervals, yet a non-significant decrease ($p \geq 0.05$) was found comparing the three-month with the six-month follow-up periods. **Table 3**

Table 3. Showing means of VAS of the Study group II (PRP group)

Pain scores (VAS) PRP (group II)				
	Before	1 month	3 month	6 month
Mean	8.13	3.87	3.40	3.47
SD	0.83	0.74	0.63	0.74
Min	7	3	2	2
Max	9	5	4	5
1 month	<u>0.000</u>			
3 month	<u>0.000</u>	<u>0.004</u>		
6 month	<u>0.000</u>	<u>0.050</u>	<u>0.582</u>	

Maximum Mouth Opening (MMO):

The Mean MMO score was (30.07 ± 0.26) preoperatively, increased significantly ($p \leq 0.05$) at one month (36.46 ± 0.23), 3 month (37.07 ± 0.22) and 6 month (38.07 ± 0.22) postoperatively. Although there was a significant increase ($p \leq 0.05$) in the MMO scores through all intervals, yet a non-significant increase ($p \geq 0.05$) was found comparing the three-month with the six-month follow-up periods. **Table 4**

Table 4. Showing means of MMO of the Study group II (PRP group)

MMO PRP (group II)				
	Before	1 month	3 month	6 month
Mean	30.07	36.46	37.07	38.07
SD	0.26	0.23	0.22	0.22
Min	29.7	36.1	36.7	37.7
Max	30.5	36.8	37.4	38.4
1 month	<u>0.000</u>			
3 month	<u>0.000</u>	<u>0.000</u>		
6 month	<u>0.000</u>	<u>0.000</u>	<u>1.000</u>	

Group III (iPRF group):**VAS scores:**

The Mean VAS score was (8.27 ± 0.88) preoperatively, decreased significantly ($p \leq 0.05$) at one month (2.80 ± 0.68), three months (1.87 ± 0.64) and six months (1.80 ± 0.56) postoperatively. Although there was a significant decrease ($p \leq 0.05$) in the VAS scores through all intervals, yet a non-significant decrease ($p \geq 0.05$) was found comparing the three-month with the six-month follow-up period. **Table 5**

Table 5. Showing means of VAS of the Study group III (i-PRF group)

Pain scores (VAS) iPRF (group III)				
	Before	1 month	3 month	6 month
Mean	8.27	2.80	1.87	1.80
SD	0.88	0.68	0.64	0.56
Min	7	2	1	1
Max	9	4	3	3
1 month	<u>0.000</u>			
3 month	<u>0.000</u>	<u>0.000</u>		
6 month	<u>0.000</u>	<u>0.000</u>	<u>0.334</u>	

Maximum Mouth Opening (MMO):

The Mean MMO score was (30.52 ± 0.82) preoperatively and increased significantly (p≤ 0.05) at one month (39.83 ± 0.18), three months (40.24 ± 0.23) and six months (41.09 ± 0.18) postoperatively. Also, the significant increase (p≤ 0.05) of the MMO score was found throughout the comparison of all the follow up intervals together. **Table 6**

Table 6. Showing means of MMO of the Study group III (i-PRF group)

MMO i-PRF (group III)				
	Before	1month	3 month	6 month
Mean	30.52	39.83	40.24	41.09
SD	0.82	0.18	0.23	0.18
Min	29	39.5	39.9	40.9
Max	31.51	40.1	40.61	41.4
1 month	<u>0.000</u>			
3 month	<u>0.000</u>	<u>0.000</u>		
6 month	<u>0.000</u>	<u>0.000</u>	<u>0.000</u>	

Comparing VAS scores of the three study groups:

When the three study groups were compared to each other's the VAS scores variation between them was statistically non-significant (p ≥ 0.05) preoperatively, while at one month, three months and six months postoperatively there was a significant decrease (P ≤ 0.05) at the VAS scores with best results for group III followed by group II in comparison with control group I. (Fig.7)

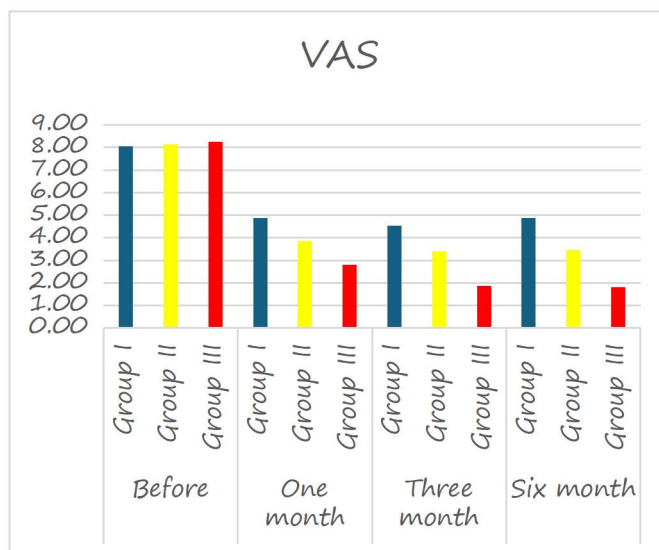


Figure 7. Showing means of VAS scores of the three groups at different time intervals.

Comparing MMO scores of the three study groups:

When the three study groups were compared to each other the Maximum Mouth Opening (MMO) scores variation between them was statistically non-significant (p ≥ 0.05) preoperatively, while at one month, three months, and six months postoperatively there was a significant increase (P ≤ 0.05) at the MMO scores with best results for group III followed by group II in comparison with control group I. (Fig.8)

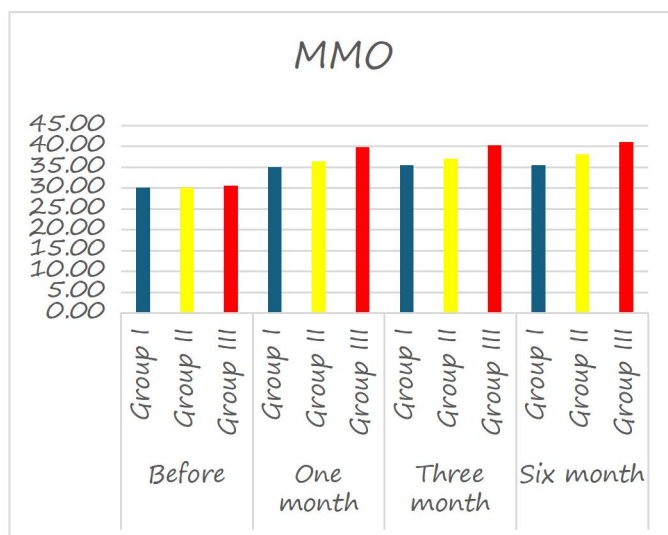


Figure 8. Showing means of MMO scores of the three groups at different time intervals.

4. Discussion

Osteoarthritis of the temporomandibular joint (TMJ-OA) is a degenerative joint condition of the TMJ that is characterized by synovitis and erosive alterations

of the articulating surfaces.¹⁻⁴ Damage to the surrounding tissues and cartilage is the hallmark of the condition, which is clinically exhibited by discomfort, aberrant joint noises, and function loss. It is thought that increased mechanical loading and a decrease in the articular cartilage's capacity for adaptation are the main elements that lead to TMJ-OA development.^{15, 30} Treatment strategies are therefore focused on enhancing the biological and mechanical characteristics of TMJ structures.^{10,1}

Research have demonstrated the effectiveness of nonsurgical treatment for TMJ osteoarthritis, including occlusal splints, physiotherapy, medication, arthrocentesis, and intraarticular injections.³¹⁻³⁴ TMJ arthrocentesis has been shown to have better outcomes than the other nonsurgical options, with success rates as high as 68% to 81%.^{2, 13,35-37} According to recent studies, arthrocentesis plus intra-articular injections of different medicines is a better combination for managing TMJ disorders than arthrocentesis alone.^{9, 6, 26 38, 39} Therefore, the current study utilized the technique of TMJ arthrocentesis in the control group & compared it to the combination of arthrocentesis & intraarticular injection.

Autologous blood is processed to create platelet-rich plasma (PRP), which is a high platelet concentration three to eight times higher than normal. It's thought that the abundance of growth factors present in this high concentration of platelets aids in tissue healing. Because PRP has both palliative and anti-inflammatory qualities, its use in treating TMJ-OA has grown in prominence recently.^{9, 15, 16, 39}

Nevertheless, anticoagulants, which are known to inhibit the healing process of wounds, must be used during the PRP preparation process. Another drawback of PRP is its preparation process's unpredictability, which can alter its leukocyte composition and growth factor release.^{21, 40} Because of these facts, platelet rich fibrin (PRF), a second-generation platelet concentrate, has been developed.¹⁸ A novel liquid formulation of injectable platelet-rich fibrin (i-PRF) was introduced by the low speed centrifugation approach, which enhanced the cell population's content and made it easier for growth factors to be released.^{40, 41} When combined with arthrocentesis, the application of i-PRF demonstrated

promising outcomes in the treatment of TMJ disorders.^{21-24, 26, 42}

In a clinical trial, *Mohi Eldin et al. 2019*⁴³ assessed the efficacy of i-PRF against PRP in the treatment of sacroiliac joint dysfunction. To the best of our knowledge, however, there are no data comparing their impact on TMJ-OA. Therefore, this study aimed to compare the effect of PRP & i-PRF in conjunction with arthrocentesis in comparison to arthrocentesis in management of TMJ- OA.

According to the current study's findings, patients with TMJ-OA who underwent arthrocentesis alone, arthrocentesis + PRP, or arthrocentesis + i-PRF saw a significant improvement in pain and MMO. However, when compared to arthrocentesis alone, the combinations of arthrocentesis + PRP & arthrocentesis + i-PRF demonstrated noticeably improved outcomes. These results are consistent with multiple studies that found that intraarticular injections combined with arthrocentesis were a more beneficial treatment for patients with TMJ-OA than arthrocentesis alone.^{15, 9, 26, 44}

When comparing the two intervention groups, it was shown that for the treatment of TMJ-OA, arthrocentesis plus i-PRF was more effective than arthrocentesis plus PRP. This conclusion is similar to the findings of a clinical trial on sacroiliac joint dysfunction conducted by *Mohi Eldin et al.*⁴³, which found that patients who got i-PRF saw a higher reduction in pain than those who received PRP.

According to the current study's results, individuals with TMJ-OA who had arthrocentesis plus i-PRF demonstrated a substantial improvement in pain and movement disorder management when compared to those who received arthrocentesis alone. The findings align with the research published by *Gozde Isik et al.*²⁶ The present study assessed the effect of intraarticular injection of i-PRF & PRP in conjugation with arthrocentesis in management of TMJ-OA. The results proved the hypothesis that i-PRF had better outcomes than PRP. Nevertheless, additional histological and radiographic analysis may be required in subsequent research to demonstrate its restorative impact and association with clinical outcomes. Additionally, more

clinical research is advised to contrast the results of i-PRF with those of other intraarticular injections, such as hyaluronic acid, corticosteroids, and analgesics.

4 Conclusion

Intraarticular injection of i-PRF following arthrocentesis is a successful treatment with better comparable reported results than intraarticular injection of PRP following arthrocentesis in management of TMJ OA.

Authors' Contributions

All authors have read and approved the manuscript.

Conflict of interest

The authors declare that they hold no competing interests.

Funding

The research study was self-funded by the authors.

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