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Original Article

Treatment of temporomandibular joint disc displacement using arthrocentesis combined with injectable platelet rich fibrin versus arthrocentesis alone

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KEYWORDS

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Abstract *Background/purpose:* Temporomandibular joint disc displacement is the most frequently reported temporomandibular disorder that may severely impair quality of life and can be challenging to treat. This study aimed to evaluate and compare the efficiency of intra-articular injection of injectable platelet rich fibrin (i-PRF) following arthrocentesis or arthrocentesis alone in treatment of patients with TMJ disc displacement with reduction.

Materials and methods: Forty patients for a total of forty joints with reducible anterior disc displacement, as confirmed by Magnetic Resonance Imaging (MRI) were selected and divided into 2 equal groups. In group I (control group), arthrocentesis alone was performed with Ringer solution. In group II (study group), a combination of arthrocentesis and intra-articular injection with 1.5 ml i-PRF was performed. The outcome variables included pain intensity evaluated with a visual analogue scale, inter-incisal opening, lateral movement evaluated in millimeters, and clicking. Assessments were done pre-operatively, and 1 week, 3 months, and 6 months postoperatively.

Results: There was statistically significant reduction in pain intensity and clicking sound and increase in mouth opening and lateral movement in i-PRF group when compared to arthrocentesis group. In addition, the differences between preoperative and postoperative status in all the measured parameters were statistically significant within the study and the control group throughout the postoperative period.

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Conclusion: The combination of i-PRF with arthrocentesis is a safe and effective method in the treatment of TMJ disc displacement with reduction.

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Introduction

The internal derangements (IDs) are considered as the most common non-inflammatory disorders of the TMJ, since they affect about 10% of the population worldwide^{1,2} and represent approximately 41.1% of all temporomandibular disorders.³ The term “internal derangement” refers to abnormal pathways during the functional movement of the TMJ that mostly involves the articular disc function, however, IDs could be observed even in asymptomatic individuals.⁴ In TMJ disc displacement, an alteration in the contact between the articulating surfaces occurs, leading to disruption of cartilage homeostasis in addition to osteoarthritic changes in some patients, which can be attributed to overload, severe wear, and inferior adaptability.⁵

Currently, management of TMJ internal derangements is concerned with relieving pain during function and achieving normal range of mandibular movements.^{3,5} For restoring the balance of the TMJ system, several treatment options are suggested, including conservative treatments⁶ such as diet regulation, antidepressant drugs/non-steroidal anti-inflammatory drugs (NSAIDs), physiotherapy, and splints. Additionally, surgical techniques like arthrocentesis, arthroscopy, and open joint surgeries are also considered.^{7,8}

Arthrocentesis is considered the minimally invasive surgical intervention that can be done as a first line of treatment in patients who are resistant to conservative treatment, aiming at removing the inflammatory mediators, restoring the synovial fluid viscosity, eliminating the adhesions, and helping joint mobility.^{9–11} It can be performed with or without intra-articular injections of several drugs.^{12,13} On the other hand, intraarticular injection can be administered independently of arthrocentesis.^{1,14} Various agents can be used for intra-articular injection inside the TMJ including hyaluronic acid (HA), steroids, platelet rich plasma (PRP) and ozone.^{15,16}

Platelet rich plasma is bio-supplement for TMJ derangement that can be considered as the first-generation platelet concentrate, obtained by blood centrifugation. It is formed of a weak fibrin network in a liquid or gel form used after activation by thrombin and calcium.¹⁷ Its anti-inflammatory, analgesic, and antibacterial properties were approved.¹ Unfortunately, the preparation of PRP requires additional use of anti-coagulants which are known suppressants to the wound healing process. As a consequence, platelet rich fibrin (PRF) was developed as a second-generation platelet concentrate.¹⁸

The implementation of PRF in 2001 is considered the first step toward the generation of blood derived PRF matrices without adding any anticoagulants.¹⁹ Conventional PRF comprises a 3-dimensional fibrin matrix

following centrifugation, and the low speed centrifugation concept has developed a new liquid formula of PRF that could be obtained for injectable purposes without adding anti-coagulants.¹⁸

A novel low speed centrifugation method resulted in the innovation of injectable PRF (i-PRF) that's a liquid formula of PRF. It stays in a liquid form for several minutes following centrifugation and thereby could be injected. It has high ability to release large concentrations of various growth factors, induce fibroblastic migration and expression of PDGF, TGF- β , and collagen1 thus provides a good environment for regeneration and repair of the tissues.^{19,20}

Because of its biological potential, it was a field of interest to assess the efficacy of intra-articular i-PRF injections after arthrocentesis compared to arthrocentesis alone in management of patients with TMJ disc displacement with reduction.

Materials and methods

Patient selection and study design

This study included forty patients suffering from TMJ internal derangement with reduction. They were all selected from the outpatient clinic of the Oral and Maxillofacial Surgery Department, Faculty of Dentistry, Mansoura University. All the included patients showed resistance to conservative treatment and recorded persistent restriction of mouth opening as well as TMJ pain and clicking.

Patients suffering from inflammatory or connective tissue diseases, neurologic disorders, history of bony or fibrous adhesion, gross mechanical restrictions and condylar fractures, previous TMJ surgery, TMJ ankylosis, or acute infection were all excluded. Moreover, patients maintained on anti-coagulants, muscle relaxants, non-steroidal anti-inflammatory drugs within 48 h preoperatively, corticosteroid injection at treatment site within one month or systemic use of corticosteroids within 2 weeks was also excluded in this study.

Pre-operative stage

Following the Declaration of Helsinki on medical protocol and ethics, this study obtained the approval of the Ethical Review Board of Mansoura University (No. A15060721). All patients were informed about the nature of the study, the risks as well as the benefits of the procedure and have signed written informed consents for the treatment plan. A detailed questionnaire by the examiner was recorded for each patient including: personal data, chief complaint, medical as well as past dental histories.

Clinical diagnosis

The following parameters were assessed for each patient:

- A. Pain was assessed using visual analogue scale (VAS): which ranges from zero to 10 (where zero refers to no pain, 1:3 mild pain, 4:6 moderate pain, 7:9 severe pain and 10 maximum pain).
- B. Clicking was assessed as its presence or absence where zero refers to absence of clicking, 1 indicates decrease in sound and frequency of clicking, and 2 indicates presence of clicking.
- C. Maximum inter-incisal opening (MIO): measured by Vernier caliper in millimeters (mm) as the vertical distance between the incisal edges of maxillary and mandibular central incisors.
- D. Range of lateral mandibular excursions was also measured using Vernier caliper in millimeters as the horizontal distance extending from maxillary midline to mandibular midline. This was measured by asking the patient to move the mandible to one side then to the other side to the maximum extent.

Magnetic resonance imaging (MRI)

For each patient, the clinical diagnosis of disc displacement with reduction was confirmed by MRI.

Operative stage

Preparation of the surgical field and injection of local anaesthesia

A reference line was traced between the lateral canthus of the eye and the tragus of the ear. Afterwards, manual palpation of the lateral edge (deepest concavity) of the articular fossa was done, which is estimated to be about 10 mm anterior to the tragus and 2 mm below the canthus-tragus line. The patient was then instructed to open wide his mouth. After painting the surgical field with antiseptic swap, 0.3 ml of local anesthetic agent Mepecaïne- L (Mepevacaine Hcl with Levonordefrin, Alexandria Co. For Pharmaceuticals, Alexandria, Egypt) was infiltrated into the area of joint penetration.

Patients grouping

Patients were randomly divided into 2 equal groups (20 patients each): Group I: patients treated with arthrocentesis alone. Group II; patients treated with a combination of arthrocentesis and intra-articular i-PRF injection.

Group I: (control group) For all patients in this group, arthrocentesis was performed in the upper joint space as follows: two guiding points were marked on the skin; the first point was 10 mm anterior to the tragus of the ear and 2 mm inferior to the canthus-tragus line, whereas the second one was marked 20 mm anterior to the tragus of the ear and 6 mm inferior to the canthus-tragus line.

Afterwards, the patient was asked to widely open his mouth, with the mandible held in the protruded position, a

20-gauge needle was inserted at the first point and 2 mL of lactated Ringer solution was injected into the superior space of the TMJ. Then a second needle of the same gauge was inserted at the second point, and 100 mL of 5% lactate solution was irrigated through the first needle inside the joint under pressure, so that the outflow of the pressurized solution occurs through the second needle.

Throughout the whole procedure, the patient was asked to move the jaw in order to optimize the flow of the solution. Finally, the needles were removed and the mandible was gently manipulated in the protrusive, vertical and lateral excursion movements to free up the articular disc.

Group II (study group): In addition to arthrocentesis which was performed as in group I, intra-articular i-PRF was injected in the joint. Liquid platelet-rich fibrin was obtained by blood collected from the antecubital vein under an aseptic condition. Utilizing butterfly needle sets and vacuum tubes (sterile uncoated 9 ml plastic tubes) without additives, the collected blood was immediately centrifuged in Spin plus centrifuge machine (TC-SPINPLUS-6 Digital Desktop Centrifuge with 3074 RCF, 100–5000 rpm, LCD Display, Includes 15 ML X 6 Rotor, Timer 15 sec-99 min, Topscien, Ningbo, China) at 700 rpm for 3 min (60 g force).¹² After centrifugation, the red blood cells were obtained as the bottom layer and the liquid PRF as the top layer in the tube, with a 7:2 approximate relation respectively.

In this group, the second needle was removed without removing the first one and a maximum dose of 1.5 ml of i-PRF was injected inside the joint.

Afterwards, the syringe was removed and similarly to the first group, the mandible was gently manipulated in protrusive, vertical and lateral excursion movements to free up the articular disc.

Post-operative stage

Patient's instructions

Patients were instructed to take soft diet, apply moist heat and keep on mandibular exercises (mouth opening as well as protrusive and lateral excursive movements) four times a day.

Medications

To reduce the risk of infection, antibiotics were prescribed for all the patients in both groups; Amoxicillin/Clavulanate Potassium 1 g tablet (Augmentin: each tablet contains 875 mg amoxicillin as amoxicillin trihydrate and 125 mg clavulanic acid as potassium clavulanate, Medical Union Pharmaceuticals (MUP), Cairo, Egypt) twice daily for 5 days.

Post-operative evaluation

Follow-up was done at 1 week, 3 months, and 6 months for the following parameters:

- A. Pain was assessed using VAS.
- B. Presence or absence of TMJ sounds was recorded.
- C. Range of lateral mandibular excursions.

D. Maximum inter-incisal opening.

Statistical analysis and data interpretation

The obtained data were analyzed by IBM SPSS Statistics for Windows, Version 22.0 (IBM Corp., Armonk, NY, USA). The qualitative data were described in terms of number and percent. The quantitative non-parametric data were described using median (minimum and maximum), whereas the parametric data were described in terms of mean, standard deviation (after utilizing Shapiro–Wilk for testing normality). The threshold of significance was fixed at 5% level. When $p \leq 0.05$, results were considered significant.

Data analysis

Qualitative data

- Chi–Square test was used for comparing 2 or more groups.
- Stewart–Maxwell test was used to compare follow-up periods with variables more than 2 categories.

Quantitative data between groups

- Parametric tests: Student t-test was used to compare 2 independent groups. While the Paired t test was used to compare between 2 studied periods.
- Non-Parametric tests: Mann–Whitney U test was used to compare 2 independent groups. While Wilcoxon signed Rank test to compare between 2 studied periods.

Results

Post-operative course

This study involved 40 patients aged between 18 and 55 (mean = 28.60 ± 8.42 & 26.45 ± 8.21 with female: male ratio = 13:7 & 16:4 in group I & group II respectively) suffering from TMID (Table 1). Generally, none of the patients showed major complications, as they were satisfied with the cost and results of the treatment. Only two patients in the i-PRF group experienced transient inability to

bring their teeth to maximum inter-cuspatation in the first two days after injection, and that may be due to coagulation of liquid PRF.

Clinical results

Pain

Median values of preoperative pain were 8.0 in the control group and 6.0 in the study group. Six months post-operatively, median values of pain were 3.0 in the control group and 0.0 in the study group. Measurements of TMJ pain using VAS showed that there was statistically significant difference ($P < 0.05$) between the two groups along the evaluation intervals. Measurements of pain intensity within each group pre-operatively and throughout the follow-up intervals showed statistically significant difference between the baseline VAS score and all other scores in both groups ($P < 0.05$) (Table 2).

Clicking

Clicking was evaluated by its presence or absence represented by numbers (2: clicking present, 1: decrease in sound and frequency of clicking, 0: no clicking). Assessment of clicking showed that there was statistically significant difference ($P < 0.05$) between the two groups along the evaluation intervals. There was statistically significant difference between clicking scores at the baseline when compared to the follow-up intervals within both groups ($P < 0.05$) (Table 3).

Maximum inter-incisal opening in mm

Mean values of preoperative MIO were 36.15 ± 7.26 mm in the control group and 31.48 ± 8.52 mm in the study group. After 6 months, mean values of MIO were 43.75 ± 5.35 mm in the control group and 50.20 ± 4.63 mm in the study group. The evaluation of MIO showed that there was statistically significant difference ($P < 0.05$) between the two groups along the evaluation intervals. There was statistically significant increase in the mean values of MIO throughout the follow up intervals when compared to baseline in both groups ($P < 0.05$) (Table 4).

Lateral movements in mm

The measurements of lateral movements revealed a statistically significant difference in right and left lateral movements ($P < 0.05$) between the two groups over time along all the evaluation intervals. There was statistically significant lower baseline right and left lateral movements as compared to movements during all the three follow up intervals in both groups ($P < 0.05$) (Table 4).

Discussion

Owing to the complex anatomical and functional structure of the temporomandibular joint and the progressive nature of internal derangement, management of its internal derangement has always been considered as a challenge for the clinicians.^{21,22} The purpose of this prospective study was to evaluate a new autogenous therapeutic protocol for management of symptomatic TMJ internal derangement. The treatment protocol consisted of intra-articular

Table 1 Demographic characteristics of the studied groups.

	i-PRF group n = 20	Control group n = 20	Student t test & Chi Square test	P -Value ^d
Age/years Mean \pm SD ^a	26.45 \pm 8.21	28.60 \pm 8.42	$t^b = 0.817$	0.419
Sex			$\chi^{2c} = 1.13$	0.288
Male	4 (20.0%)	7 (35.0%)		
Female	16 (80.0%)	13 (65.0%)		

^a SD: Standard Deviation.

^b t: Student t test.

^c χ^2 : Chi Square test.

^d P value: Probability.

Table 2 Comparison of VAS score between studied groups along the treatment follow-up intervals.

Pain (VAS score) ^a Median (range)	i-PRFgroup n = 20	Control group n = 20	Mann Whitney test	P -Value ^c
Pre-operative	6.0 (4.0–10.0)	8.0 (3.0–9.0)	Z ^b = 1.49	0.134
After one week	0.0 (0.0–2.0)	5.0 (1.0–8.0)	Z = 12.62	<0.001*
After 3 months	0.0 (0.0–0.0)	3.0 (1.0–6.0)	Z = 12.09	<0.001*
After 6 months	0.0 (0.0–2.0)	3.0 (1.0–5.0)	Z = 9.79	<0.001*
Wilcoxon signed rank test	P1 ^d < 0.001* P2 ^e < 0.001* P3 ^f < 0.001*	P1<0.001* P2<0.001* P3<0.001*		

^a VAS: Visual Analogue Scale.

^b Z: Mann Whitney test.

^c P value: Probability.

^d P1: difference between pre-operative and after one week.

^e P2: difference between pre-operative & after 3 months.

^f P3: difference between pre-operative & after 6 months follow up.

injections of i-PRF after arthrocentesis and evaluation of its effect compared to arthrocentesis alone.

Arthrocentesis of TMJ is considered as the simplest form of surgery for management of its internal derangement. It may remove catabolites as well as inflammatory cells, and moreover, it increases the maximum inter-incisal opening by relieving the adhesions.²³ In this study, we found significant increase in MIO and lateral movement with significant decrease in joint pain and clicking between baseline and 6 months follow up within the arthrocentesis group. Our result was in accordance with Neeli et al.²⁴ and Leibur

et al.²⁵ Also, this was in accordance with Hancı et al.²¹ who showed significant increase in mouth opening at 6 months with arthrocentesis and stated that arthrocentesis was effective in the late term results due to removal of the articular adhesions and expanding the articular space which in turn causes muscles relaxation and tissue contraction.²⁶ Besides, many studies have reported the effectiveness of arthrocentesis to be up to 91%, including displacement without reduction.^{13,26}

Many studies evaluated the efficacy of some drugs or autologous products after TMJ arthrocentesis procedure to relieve symptomatic internal derangements and improve the quality of life of the patients.²⁶ Hyaluronic acid,^{7,10} steroids²⁷ NSAIDs²⁸ and morphine were injected into the joint either alone or in combination.^{11,29} and proved neither reversal nor permanent cessation of the deterioration cycle of the derangement.³⁰

Considering the complications such as allergic reactions and infection²⁶ on addition to understanding the deterioration mechanism that occurs in the TMJ, bio-supplementation approaches with ortho-biological agents like platelet-rich biomaterials have become popular in the management of ID.^{9,22} Many researchers have managed TMJ internal derangement by PRP injection, since it can stimulate release of endogenous HA, growth factors as well as joint angiogenesis. Nevertheless, contradicting results about PRP effectiveness^{22,31} and its insignificant benefit have been recorded.^{11,32}

Liquid PRF biomaterial formulations have been prepared recently with low-speed centrifugation for injectable purposes. They have become popular due to their simple preparation technique, that does not require the addition of either anticoagulants or activators. Meanwhile, the evidence of their efficacy in TMJ internal derangement is still limited.^{1,33}

In the present study, there was statistically significant difference between the i-PRF group and the control group regarding pain, maximum inter-incisal opening and lateral movement. In addition, there was statistically significant difference regarding all these studied parameters within the i-PRF group between baseline and 6 months follow up. Our results agreed with Yuce et al.,³³ who compared the efficacy

Table 3 Comparison of clicking score between studied groups along the treatment follow up intervals.

Clicking number (%)	i-PRF group n = 20	Control group n = 20	Monte Carlo test (P -Value ^a)
Pre-operative			
2	20 (100%)	20 (100%)	P = 1.0
After one week			
0	15 (75.0%)	7 (35.0%)	<0.001*
1	5 (25.0%)	1 (5.0%)	
2	0	12 (60.0%)	
After 3 months			
0	15 (75.0%)	10 (50.0%)	0.029*
1	5 (25.0%)	4 (20.0%)	
2	0	6 (30.0%)	
After 6 months			
0	12 (60%)	10 (50.0%)	0.0006*
1	8 (40.0%)	1 (5.0%)	
2	0	9 (45.0%)	
Stewart Maxwell test	P1 ^b < 0.001* P2 ^c < 0.001* P3 ^d < 0.001*	P1 = 0.005* P2<0.001* P3<0.001*	

^a P: Probability.

^b P1: difference between pre-operative and after one week.

^c P2: difference between pre-operative & after 3 months.

^d P3: difference between pre-operative & after 6 months follow up.

Table 4 Comparison of MIO and lateral movement between studied groups along the treatment follow up intervals.

	i-PRF group n = 20	Control group n = 20	P -Value ^b between i-PRF & control (Student t test)	P -Value ^b within i-PRF group (Paired t test)	P -Value ^b within control group (Paired t test)
MIO^a					
Pre-operative	31.48 ± 8.52	36.15 ± 7.26	0.07	P1 ^c < 0.001*	P1 = 0.005*
After one week	44.70 ± 6.48	40.40 ± 5.2	0.032*	P2 ^d < 0.001*	P2 < 0.001*
After 3 months	48.25 ± 4.85	42.40 ± 5.21	0.001*	P3 ^e < 0.001*	P3 < 0.001*
After 6 months	50.20 ± 4.63	43.75 ± 5.35	< 0.001*		
RLM^f					
Pre-operative	6.15 ± 2.78	6.53 ± 1.94	0.624	P1 ^c < 0.001*	P1 < 0.001*
After one week	9.75 ± 8.30	8.30 ± 1.38	0.003*	P2 ^d < 0.001*	P2 < 0.001*
After 3 months	11.15 ± 1.31	8.53 ± 1.73	< 0.001*	P3 ^e < 0.001*	P3 = 0.001*
After 6 months	11.85 ± 1.84	8.68 ± 2.0	< 0.001*		
LLM^g					
Pre-operative	7.15 ± 3.15	7.13 ± 2.25	0.977	P1 ^c = 0.004*	P1 = 0.007*
After one week	10.0 ± 2.49	8.55 ± 1.98	0.049*	P2 ^d = 0.003*	P2 = 0.003*
After 3 months	10.65 ± 2.49	9.22 ± 1.65	0.04*	P3 ^e < 0.001*	P3 = 0.001*
After 6 months	11.55 ± 2.43	9.5 ± 1.47	0.003*		

^a MIO: Maximum interincisal Opening.

^b P value: Probability.

^c P1: difference between pre-operative and after one week.

^d P2: difference between pre-operative & after 3 months.

^e P3: difference between pre-operative & after 6 months follow up.

^f RLM: Right Lateral Movement.

^g RLM: Left Lateral Movement.

of arthrocentesis alone, arthrocentesis followed by HA injection, and arthrocentesis followed by i-PRF injection and revealed significant decrease in pain and increase in maximum inter-incisal opening in the study group. Similarly, Hancı et al.²¹ reported that intra-articular PRP injection was more effective than arthrocentesis. Torul et al.,³⁰ showed that injection of i-PRF appeared to have significant long-term promising effects in the management of TMJ internal derangement which can be related to its ability to selectively enrich leukocytes, platelets, growth factors and cytokines within its liquid matrices.^{1,18,19,33} Our results disagreed with Albilal et al.¹ where no statistically significant decrease in pain score was obtained in the i-PRF group and the increase in maximum mouth opening was insignificant for all patients.

Regarding the clicking sound, there were statistically significant difference between both groups. Also, there was statistically significant decrease in the clicking sound between baseline and 6 months follow-up in the study group during the follow-up period. This result was in accordance with Al-Delamye et al.³¹ In contrast, Hassan et al.³⁴ who used PRP, showed that there was no significant difference when comparing joint sounds all over the follow-up period. Also Moon et al.³⁵ emphasized that PRP was effective in the treatment of TMJ pain and restricted mouth opening, but it was not effective in the treatment of clicking. In the present study, we suppose that clicking disappearance may be due to the lubricating action of i-PRF after coagulation within 15 min from injection.

In the present study, a single injection of i-PRF into the joint was done following arthrocentesis. This was different

than Albilal et al.¹ who performed multiple injections with 2 weeks intervals until an acceptable improvement was observed and Yuce et al.³³ who applied three consecutive injections weekly. Our study was similar to Torul et al.³⁰ and Karadayi et al.²⁶ who used single injection of i-PRF in addition to arthrocentesis and observed promising results regarding postoperative pain, clicking and mouth opening. This may be due to the sustained growth factors release from its matrices which eliminates the need for subsequent injections. Besides, administering single injection to all patients ensured that they all received standardized dose.

At the end of the follow-up period, all patients were satisfied with the cost of treatment and pain regression. While in study carried out by Kraus et al.³⁶ following physical therapy, only 76% of the patients recorded satisfaction with the obtained results.

From the results of our study, we concluded that additional intra-articular i-PRF injection following arthrocentesis has proved to be more effective than arthrocentesis alone for the management of internal temporomandibular derangement. Improved functional outcomes and quality of life have been documented.

Declaration of competing interest

The authors have no conflicts of interest relevant to this article.

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