

EVALUATION OF ARTHROCENTESIS WITH AND WITHOUT PLATELET RICH PLASMA INJECTION IN PATIENTS WITH DISC DISPLACEMENT WITH REDUCTION. A RANDOMIZED CONTROLLED CLINICAL TRIAL

Mohammad Ibrahim Mahmoud Alhoor*, Walaa Kadry** and Yasmine Nassar**

ABSTRACT

Objectives: The current study aimed to assess the effect of arthrocentesis followed by injection of platelet rich plasma (PRP) versus arthrocentesis in the management of anterior disc displacement with reduction (DDWR) disorder.

Materials and methods: Seventy-four patients (mean age 29.3 years) with anterior DDWR were randomized and divided according to a predetermined eligibility criteria into two equal groups: arthrocentesis (control) and arthrocentesis with PRP injection (study). For both groups, Pain intensity was assessed using visual analogue scale and maximum mouth opening (MMO) preoperatively, immediate, 1 week, 1 month, 3 and 6 months postoperatively. Moreover, the disc displacement angle was recorded preoperative and after 6 months.

Results: Pain was significantly reduced in the study group compared to the control group only at 1 week, 1 month, 3 and 6 months ($p < 0.05$). However, there was non significant difference among groups regarding MMO at all time intervals or disc position angle after 6 months ($p > 0.05$).

Conclusions: PRP resulted in pain reduction for most of the period of follow up, with no apparent positive effect on MMO or disc position.

Clinical Relevance: The study evaluates whether the anti-inflammatory and growth stimulation effect of PRP is reflected on reduction of pain intensity and disc position in the management of patients suffering from DDWR. **Clinical trial registration NCT05983653**

KEYWORDS: Platelet rich plasma, internal derangement, arthrocentesis, temporomandibular joint.

* Principal Researcher At Oral and Maxillofacial Surgery Department, Faculty of Dentistry, Cairo University, Cairo, Egypt

** Associate Professor at Oral and Maxillofacial Surgery Department, Faculty of Dentistry, Cairo University, Cairo, Egypt.

INTRODUCTION

Anterior disc displacement with reduction (DDWR), is a common temporomandibular disorder that induces orofacial pain with 73.2% prevalence in females^[1]. The patients usually present complaining of TMJ sounds and limited jaw movements. All these symptoms are yielded from articular disc stretching away from its attachment to the articular surfaces. The main goal of the current treatments of DDWR is to relieve symptoms of joint discomfort and improve the mandibular range of motion.. According to TMJ dysfunction degree, several treatment protocols were utilized starting from medications, splint therapy, physical exercises to minimally invasive (arthrocentesis and arthroscopy), and open surgical procedures^[2-4]. Ideal treatment of DDWR is controversial, however, conservative and reversible treatments should be attempted first before deciding to perform an irreversible surgery if deemed essential.

Participants who were refractory to the conservative treatments, minimally invasive techniques are widely accepted as first-line treatments^[5,6].

Arthrocentesis is considered a minimally invasive management option for DDWR cases who are refractory to the conservative options such as medication, soft diet, appliances, and physiotherapy as electro/physiotherapy (mega pulse, ultrasound, soft laser, and acupuncture)^[7]. Recent literature indicates that arthrocentesis is a successful option for the improvement of DDWR related symptoms. It eliminates the inflammatory mediators which assists in the increase of range of motion with allivation of pain and other symptoms rather than the eliminating the underline cause^[8].

Recent clinical trials, that suggested that arthrocentesis combined with various therapeutic agents like hyaluronic acid, steroids, nsaid, have provided superior results, didn't actually prevent the deterioration sequele of internal derangement process^[9]. PRP comprises various

concentrated growth factors which assists tissue regeneration, induces anti-inflammatory and analgesic effect through the whole healing process leading to improvement in function^[9]. Following activation, platelets release active proteins which stimulate cellular attraction, neovascularization, morphogenesis and fibroblast growth following their binding to target cell receptors^[10,11]. In the current study, the synergistic combination of arthrocentesis with PRP is compared to arthrocentesis alone in the management of DDWR.

Moreover, PRP is necessary for blood clotting and hemostasis, and has an analgesic effect by releasing four peptides activated by proteases. On injection, the activated platelets release different proteins like angiopoietin, endostatin, platelet factor 4, and growth factors like platelet-derived growth factor (PDGF) and vascular endothelial growth factor (VEGF), all of which stimulate cell proliferation and stem cell recruitment which are essential for healing^[12].

TMJ lavage followed by platelet rich plasma (PRP) injection was used with variable results. Literature search have shown encouraging results using PRP in the management of DDWR disorder^[13].

Adding to absence of PRP side effects, it can minimize pain and inflammation, enhance joint function via stimulation of cartilage matrix repair and increase hyaluronic acid synthesis where injury occurs^[14,15].

PRP was utilized for DDWR management in several studies compared to various therapies with good results.^[16-20] Recently, there has been insufficient data to compare different therapies, and thus establish priorities for their use. Heterogeneity in preparations and agents' combinations is a major limitation in determining treatment efficacy. Besides,

MRI is considered the gold standard imaging tool for assessment of soft tissue abnormalities of the

TMJ, masticatory muscles as well as determining the condyle- disc relationship^[21]. It is a non-invasive diagnostic method that enables quantitative and qualitative assessment of the structures within the joint, including relation and position between these structures^[22].

There is little evidence that arthrocentesis or arthrocentesis with PRP injections is better than other therapies. Moreover, assessment of disc displacement angle was assessed following PRP injection in few reports [23, 24] which necessitates further research. Therefore, the purpose of the current study is to compare arthrocentesis to arthrocentesis with PRP injection in the management of DDWR and evaluate disc position changes after 6 months from the two interventions.

PATIENTS AND METHODS

Study Design

The current research was compliant with the guidelines of the institutional ethical review board that follows declaration of Helsinki guidelines. The current randomized control clinical trial was conducted in accordance to the CONSORT guidelines. Patients with anterior disc displacement with reduction who were retrieved from the department of Oral and Maxillofacial Surgery, Faculty of Dentistry, Cairo University were assessed for eligibility. Eligible patients' age ranged from 18-44 years. An informed consent was obtained from each patient.

Method of collection & Randomization

Seventy-four participants with anterior DDWR who were eligible were randomly assigned into two equal groups: The control group (n=37) was managed via arthrocentesis and the test group (n=37) with arthrocentesis followed by PRP injection. Before the intervention, the management protocol including treatment and postoperative care was provided and potential complications were

discussed with each participant. Patients were also informed that they could withdraw anytime from the research. The same operator provided the treatment for all patients under local anesthesia.

Online randomizer (www.random.org) was used for random patient allocation. A minimum sample of seventy-four patients (37 per group) was necessary to detect the difference in treating anterior disc displacement with reduction using arthrocentesis with PRP and arthrocentesis. Chi-square- test was used with 95% confidence level and 80% power (PASS program, version 23).

Eligibility criteria

Healthy adults were selected to participate in this study according to predefined inclusion criteria which is: Wilkes stage II (chronic pain combined with average range of motion of anterior DDWR or painful joint noises associated with mouth opening and/or closure as evident by the clinical and MRI findings of DDWR that didn't respond to the conservative therapy). Patients who had previous TMJ surgery, medical history of systematic disease or those participating in other studies were excluded.

Preoperative patient assessment

A comprehensive history was obtained followed by detailed clinical examination for all patients. It included assessment of pain using visual analog scale (VAS), presence of joint noise, measurement of maximum mouth opening (MMO) in millimeters. All preoperative measurements were recorded. Preoperative TMJ (T1 & T2) MRI images, in open and closed position were requested for each patient.

Intraoperative procedures

For all patients and along the canthotragal line (from the lateral canthus of the eye to the mid-tragus), two points were marked on the skin surface. The posterior point was 10 mm from the tragus and 2 mm below the that line while the anterior one was 10 mm from the first point and 10 mm below

the Canthotragal line. Subcutaneous Infiltration anesthesia followed by auriculotemporal nerve block was given (Mepecaine L). The pre-auricular area was disinfected using 10% Betadine, followed by 70% alcohol.

Patients were instructed to maintain the mouth opening during lavage that was assisted by placement of bite block. An 18-gauge needle was intruded into the superior joint space through the posterior inlet point followed by saline injection (2ml) to distend the joint space. Rebound pressure on the syringe piston and flow back of few saline drops were indicators of accurate needle position at the entry point. Another 18-gauge needle was inserted in the outlet point. Lavage of the superior joint space was then performed with 150 ml saline to establish a steady solution flow, through which the patient was instructed to move the mandible (opening, protrusive, and lateral movements) to facilitate the free flow.

For the study group, 10 mm of autologous venous blood was aspirated from the median cubital vein. The blood was then drawn into glass tubes containing 3.2% sodium citrate (anticoagulant agent). Finally, the tubes were placed inside the centrifuge device (China, model 80-1). Centrifugation was set to 1000 RPM for 10 minutes. One ml of the yielded PRP was injected following arthrocentesis after removal of the outlet needle.^[25] (**Fig 1**)

Post-operative care & instructions

Each patient was instructed to follow a soft diet for two weeks. For increasing the mouth opening, patients were instructed to do physical exercises (tongue up, side-to-side movement, and manual stretch). Clindam300 mg and Brufen 400mg capsules were prescribed every 8 hours for five days.

VAS and MMO were recorded immediate, 1 week, 1 month and 6 months postoperative and

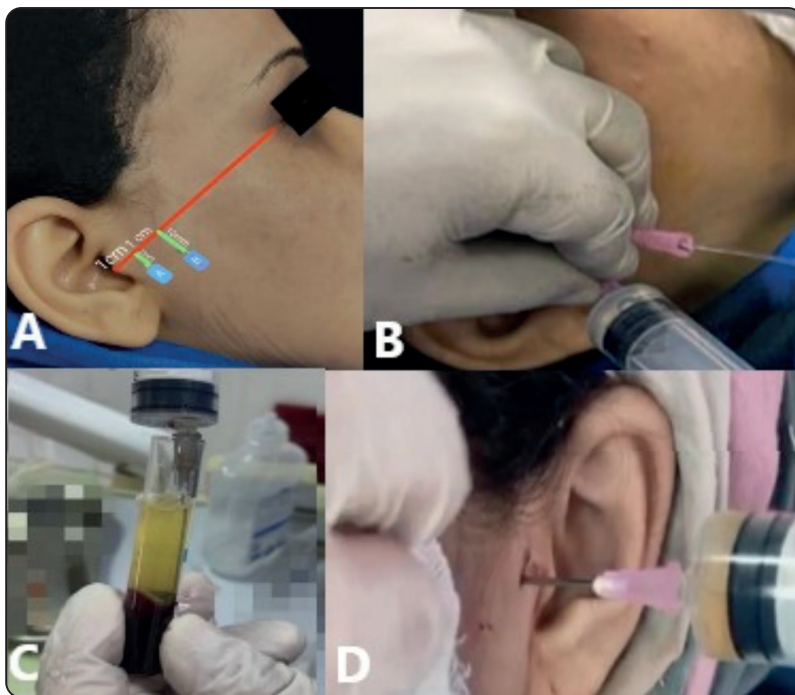


Fig. (1): A clinical photograph showing: A: Red line: cantho-tragal line, (A: posterior inlet point, B: anterior outlet points), B: Free flow of the washing solution is established, C: aspiration of PRP, D: Injection of PRP.

* Mepecaine L: 2% with Levonordefrin 1:20000

** Betadine povidine-iodine USP Nile Pharmaceuticals Co., Cairo, Egypt.

*** Clindamycin, as hydrochloride, Sigma, Egypt

**** Ibuprofen, Abbott, Egypt

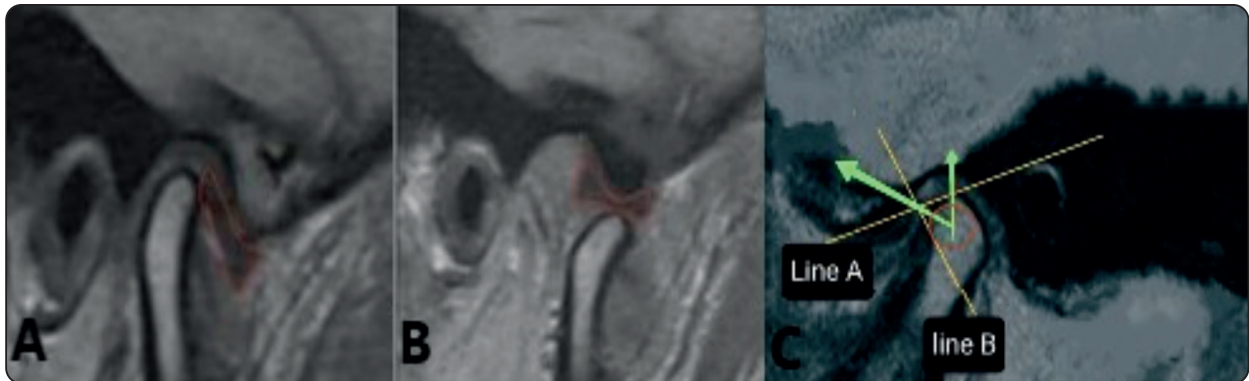


Fig. (2): MRI image of the joint reveals disc displacement with reduction (A) Anterior disc displacement on mouth closure, (B) The disc is reduced to the normal position on mouth opening, (C) In closed mouth position: Line A: From the superior margin of external auditory meatus to the articular eminence crest, line B: Posterior edge of the articular disc. The angle of disc displacement was measured between a line passing through the intersection of lines 'A' and 'B' and a line that corresponds to long axis of the condylar head [26].

documented for later analysis. MRI was ordered at 6 months to detect the disc position angle for comparison with the preoperative one. (**Fig 2**) All data was documented by another author who was blinded to the assigned group.

Statistical analysis

All patients' data were imported into soft Excel (Microsoft Corp., Redmond, Wash.), then exported to IBM SPSS software package version 20.0. (Armonk, NY: IBM Corp) for statistical analysis. Final data were represented as percent, mean, range, median (IQR) and standard deviation. Chi-square test and Mann Whitney test were utilized to compare results between the studied groups. Wilcoxon signed ranks test was utilized to compare data within the same group. To assess the normality of the continuous variables, Kolmogorov-Smirnov test was used. An alpha level was set to 5% with a 95% significance level and a beta error accepted up to 20% with 80% power of study.

RESULTS

The current study involved seventy-four participants (70 females & 4 males) with DDWR. Age of those patients ranged from 18-44 years (mean age is 29.3 years).

Patients of study group (2 males and 35 females) were managed with arthrocentesis with PRP injection while control group patients (2 males and 35 females) were managed with arthrocentesis. There was non significant difference among the studied groups regarding patient's Age "years", Gender, and Site ($P > 0.05$). **Table 1**

Pain (VAS score):

There was a statistically significant reduction in pain in the two groups from the 1st day ($p < 0.05$), also there was a statistically significant reduction in pain in arthrocentesis with PRP group than the cony group at 1 week, 1 month, 3 and 6 months, with p-value ($p < 0.05$). **Table 2**

Maximum mouth opening (MMO)

There was non- significant difference among groups regarding MMO at 1 day, 1 week, 1 month, 3 and 6 months, with p-value ($p < 0.05$). However, there was a statistically significant increase in mean of MMO for the arthrocentesis with PRP group at all time intervals from day one till the end of follow up period ($p < 0.001$). **Table 3**

Few complications like peri-auricular tissue swelling were evident and was treated with an ice-pack and antibiotic prescription. Temporary facial

TABLE (1) Patients' demographic data.

Demographic data	Arthrocentesis with PRP Group (n=37)	Arthrocentesis without PRP Group (n=37)	Test value	p-value	Sig.
Age "years"					
Mean±SD	29.30±6.86	26.95±5.97	2.475	0.120	NS
Range	18-44	19-42			
Gender					
Female	35 (94.6%)	35 (94.6%)	0.000	1.000	NS
Male	2 (5.4%)	2 (5.4%)			
Site					
Left	13 (35.1%)	23 (62.2%)	4.409	0.082	NS
Right	24 (64.9%)	14 (37.8%)			

Using: *t*-Independent Sample *t*-test for Mean±SD;

Using: χ^2 : Chi-square test for Number (%) or Fisher's exact test, when appropriate. NS: Non-significant; S: Significant; HS: Highly significant

TABLE (2) A comparison of pain score (VAS) among groups at all time intervals

Pain	Arthrocentesis with PRP Group (n=37)	Arthrocentesis without PRP Group (n=37)	Test value	p-value	Sig.
At 1 day					
Mean±SD	8.00±1.20	8.03±1.04	0.011	0.918	NS
Median (IQR)	8 (7-9)	8 (7-9)			
Range	5-10	6-10			
At 1 week					
Mean±SD	2.27±1.37	4.03±1.28	32.556	0.001	HS
Median (IQR)	2 (1-3)	4 (3-5)			
Range	0-6	2-8			
At 1 month					
Mean±SD	0.81±1.41	2.43±0.83	36.201	0.001	HS
Median (IQR)	0 (0-1)	2 (2-3)			
Range	0-5	1-5			
At 3 months					
Mean±SD	0.76±1.32	2.19±0.66	34.822	0.001	HS
Median (IQR)	0 (0-1)	2 (2-3)			
Range	0-5	1-3			
At 6 months					
Mean±SD	0.41±0.86	1.84±0.80	54.721	0.001	HS
Median (IQR)	0 (0-1)	2 (1-2)			
Range	0-4	0-3			

IQR: Interquartile range

Using: *U*=Mann-Whitney test for non-parametric data "Median (IQR)"

NS: Non-significant; S: Significant; HS: Highly significant

paralysis due to anesthesia of the facial nerve was managed by patient assurance and eye protection. It was transient and disappeared within the few hours after the procedure.

MRI assessment results of disc position

Among the studied groups, there was no statistically significant difference in the disc position at 6 months ($p>0.05$), as well as between the preoperative and 6 months disc position in both groups. *Table 4*

TABLE (3) Comparison of MMO among groups at all follow up intervals

Maximum mouth opening	Arthrocentesis with PRP Group (n=37)	Arthrocentesis without PRP Group (n=37)	Test value	p-value	Sig.
At 1 day					
Mean±SD	37.35±2.80	37.49±1.92	0.059	0.810	NS
Range	34-45	34-43			
Immediate after TTT					
Mean±SD	39.35±2.36	39.38±1.71	0.003	0.955	NS
Range	36-45	36-43			
At 1 week					
Mean±SD	39.35±2.36	39.32±1.68	0.003	0.955	NS
Range	36-45	36-43			
At 1 month					
Mean±SD	39.35±2.36	39.32±1.68	0.003	0.955	NS
Range	36-45	36-43			
At 3 months					
Mean±SD	39.35±2.36	39.32±1.68	0.003	0.955	NS
Range	36-45	36-43			
At 6 months					
Mean±SD	39.35±2.36	39.32±1.68	0.003	0.955	NS
Range	36-45	36-43			

Using: *t*-Independent Sample *t*-test for Mean±SD;

NS: Non-significant; S: Significant; HS: Highly significant

TABLE (4) Comparison between the preoperativedisc position and after 6 months.

Disc position	preoperative	At 6 months	Paired Sample t-test		
	Mean±SD	Mean±SD	MD	t-test	p-value
Arthrocentesis with PRP	70.32±11.01	71.92±10.67	-1.6	1.337	0.372
Arthrocentesis without PRP	75.51±4.18	77.32±3.17	-1.81	1.828	0.125

p-value >0.05 (insignificant); **p*-value <0.05 (significant); ***p*-value <0.001 (highly significant)

DISCUSSION

Internal derangement with or without reduction is considered as a challenge to the oral and maxillofacial surgeon. The most frequent intra-articular disorder is anterior DDWR (41%), which is usually symptom-free and needs no intervention as the TMJ structures adapt well to various disc positions and without pain. Clinically, during condylar movement, DDWR is associated with TMJ noise (clicking, snapping, and/or popping sound). However, patients with DDWR exhibit painful symptoms due to joint inflammation, muscle spasms, and loss of elasticity of retro-discal tissues [27].

The selected patients of both groups were comparable as regards age and gender. The clinical variables as pain (VAS score), MMO (vertical), and disc position were evaluated at different time points. Pain (VAS) was significantly decreased in both groups starting from 1st week follow-up with more decrease in the intensity of pain in the study group. There was significant reduction of pain intensity scores in the study group compared to the other group at 6 months indicating the advantage of injection of PRP after arthrocentesis compared to arthrocentesis alone. This might be attributed to the synergistic effect between the PRP and arthrocentesis, which eliminates inflammatory cytokines and debris from the synovial fluid, decreases friction between articular surfaces and modifies the hydraulic pressure within TMJ components. PRP has the added benefit of potentially enhancing healing, analgesia, and the removal of inflammatory mediators, as well as acting as a scaffold to facilitate the migration of stem cells [28].

VAS score results agree with Singh et al [29] and Pihut et al [5]; who reported significant effect on the reduction of pain intensity following the injection of PRP in TMJ dysfunction patients. Moreover, PRP versus hyaluronic acid efficacy in the management of Wilkes V TMJ patients was investigated by Hossameldin et al [30]. There was 65.6% success rate

in the HA group compared to 69.6% for the PRP group with non-significant difference.

Moreover, Lin et al [31]; compared arthrocentesis followed by PRP injection to PRP alone in the management of TMJ osteoarthritis (TMJ-OA) with resultant similar results for both approaches with no statistically significant difference. However, arthrocentesis combined with PRP was superior to PRP alone. This comes along with the results of our study where utilization of PRP resulted in a statistically significant pain reduction in comparison to arthrocentesis alone.

Whereas, Singh et al. [29]; had non significant difference among the studied groups at 3 & 6-month follow-up, there was significant difference in pain reduction within the same group at different Time intervals. Furthermore, Habibullah et al. [32] compared the VAS score outcome of both interventions at 3 months follow up without resultant significant difference among the studied groups. Habibullah et al attributed the non-significant result to the incompliance of the patients to the postoperative instructions

Regarding MMO, it was minimally improved immediate in both groups with constant measurements throughout the whole period of the study; without significant differences among the groups. The pre-operative mean MMO for study group was 37.35 ± 2.80 mm and 37.49 ± 1.92 mm for control group. Immediate post-operative, the average MMO for study group was 39.35 ± 2.36 mm, while control group's average was 39.38 ± 1.71 mm, which was minimally increased (2mm) with constant measurement throughout the whole study interval.

These results match with those of Singh et al [29]; who documented non significant difference in MMO among the studied groups at 1-month, 3 and 6-months post-operative. Whereas, Ghoneim et al [33]; concluded that the MMO was significantly enhanced ($p < 0.05$) in both groups from the

baseline. Hanc et al^[34], reported that the average MMO increased from 32 mm (baseline) to 39 mm (after injection) with statistically significant difference ($p=0.01$) at 6 months. Authors suggest that enhanced MMO might be attributed to complete relief of intra-articular adhesions and distention of articular space with resultant muscle relaxation.

In the present study; objective analysis of disc position and its relation to the condyle were assessed via unilateral sagittal MRI (T1-weighted) of TMJ and compared between the study groups. This quantitative data revealed non-significant difference statistically among the studied groups both preoperative and 6 months postoperative. In this context, our study revealed that the pre-procedural mean disc position for study group was 70.32 ± 11.01 , while for control group, it was 75.51 ± 9.18 . At the 6 months mark post-operative, the average disc position for study group was 71.92 ± 10.67 , while for control group it was 77.32 ± 8.17 , very minimum change in disc position in each group, and without significant difference among the two groups.

To the best of our knowledge, only two studies, that were conducted by lee and yoon [35], and Ohnuki et al [36], had evaluated disc position on MRI following arthrocentesis to treat internal derangement (DDWR). Both investigators reported that the chosen treatment did change disc position. However, in small number of cases, DDWOR turned into DDWR while no change yielded in the cases of DDWR except for improvement only of their signs and symptoms. The disc position angle might need longer follow up period to be noticed on MRI, this to permit optimum healing for intra-articular disc and attached ligaments.

In the same context, Moses et al^[37]; documented that only 8% of the DDWR cases exhibited reduction in disc position after an average of 17 months postoperatively.

To our knowledge, this is the first study to evaluate the 6 months' changes of articular disc

position and relation (angle) using MRI before and 6 months after treatment for anterior DDWR according to a protocol series.

Absence of a objective evaluation of the psychological state of patients and relatively short follow up were limitations of the present study. Although, MRI requests were standard for each patient, longer follow up period is recommended to allow sufficient healing period to be reflected on articular disc recapture on MRI.

CONCLUSION

Based on the results of the current study, authors conclude that in the anterior DDWR; PRP caused reduction in pain at in the whole period of following up via its anti-inflammatory and regenerative effect. PRP has no positive effect on disc position or MMO.

CONFLICT OF INTEREST

No conflicts of interest.

FUNDING

The research is self-funded.

Ethical approval

The study was approved by the ethics committee of the Faculty of Dentistry, Cairo University. Under the serial number 13 4 23. The trial registry was performed on clinical trial. Gov (NCT05983653)

REFERENCES

1. Bagis, B., Ayaz, E. A., Turgut, S., Durkan, R., & Özcan, M (2012) Gender difference in prevalence of signs and symptoms of temporomandibular joint disorders: a retrospective study on 243 consecutive patients. *International journal of medical sciences*, 9(7), 539–544. <https://doi.org/10.7150/ijms.4474>
2. Conti, P. C., dos Santos, C. N., Kogawa, E. M., de Castro Ferreira Conti, A. C., & de Araujo, C. dosR (2006) The treatment of painful temporomandibular joint clicking with oral splints: a randomized clinical trial. *Journal of the*

- American Dental Association (1939), 137(8), 1108–1114. <https://doi.org/10.14219/jada.archive.2006.0349>
3. Grossmann, E., Guilherme Vargas Pasqual, P., Poluha, R. L., Iwaki, L. C. V., Iwaki Filho, L., & Setogutti, Ê. T (2017) Single-Needle Arthrocentesis with Upper Compartment Distension versus Conventional Two-Needle Arthrocentesis: Randomized Clinical Trial. *Pain research & management*, 2017, 2435263. <https://doi.org/10.1155/2017/2435263>
 4. Chandrashekhar, V. K., Kenchappa, U., Chinnannavar, S. N., & Singh, S (2015) Arthrocentesis A Minimally Invasive Method for TMJ Disc Disorders - A Prospective Study. *Journal of clinical and diagnostic research: JCDR*, 9(10), ZC59–ZC62. <https://doi.org/10.7860/JCDR/2015/15045.6665>
 5. Pihut, M., Szuta, M., Ferendiuk, E., & Zeńczak-Więckiewicz, D (2014) Evaluation of pain regression in patients with temporomandibular dysfunction treated by intra-articular platelet-rich plasma injections: a preliminary report. *BioMed research international*, 132369. <https://doi.org/10.1155/2014/132369>
 6. Lana, J.F., Santana, M.H., Belangero, W.D., & Luzo, Â.C (2014) Platelet-rich plasma: regenerative medicine: sports medicine, orthopedic, and recovery of musculoskeletal injuries.
 7. Soni A (2019) Arthrocentesis of Temporomandibular Joint- Bridging the Gap Between Non-Surgical and Surgical Treatment. *Annals of maxillofacial surgery*, 9(1), 158–167. https://doi.org/10.4103/ams.ams_160_17
 8. Carvajal, W. A., & Laskin, D. M (2000) Long-term evaluation of arthrocentesis for the treatment of internal derangements of the temporomandibular joint. *Journal of oral and maxillofacial surgery: official journal of the American Association of Oral and Maxillofacial Surgeons*, 58(8), 852–857. <https://doi.org/10.1053/joms.2000.8201>
 9. Singh, A. K., Sharma, N. K., Kumar, P. G. N., Singh, S., Mishra, N., & Bera, R. N (2021) Evaluation of Arthrocentesis with and Without Platelet-Rich Plasma in the Management of Internal Derangement of Temporomandibular Joint: A Randomized Controlled Trial. *Journal of maxillofacial and oral surgery*, 20(2), 252–257. <https://doi.org/10.1007/s12663-019-01320-y>
 10. Anitua, E., Sánchez, M., & Orive, G (2010) Potential of endogenous regenerative technology for in situ regenerative medicine. *Advanced drug delivery reviews*, 62(7-8), 741–752. <https://doi.org/10.1016/j.addr.2010.01.001>
 11. Pietrzak, W. S., & Eppley, B. L (2005) Platelet rich plasma: biology and new technology. *The Journal of craniofacial surgery*, 16(6), 1043–1054. <https://doi.org/10.1097/01.scs.0000186454.07097.bf>
 12. Anitua E (1999) Plasma rich in growth factors: preliminary results of use in the preparation of future sites for implants. *The International journal of oral & maxillofacial implants*, 14(4), 529–535.
 13. Sharma, S.M, Thakar D. (2014) Clinical efficacy of autologous concentrate platelets in treatment of TMJ disorders- apilot study. *Nitte University J of Health Science* 4:70- 74.
 14. Cerza, F., Carni, S., Carcangiu, A., Di Vavo, I., Schiavilla, V., Pecora, A., De Biasi, G., & Ciuffreda, M (2012) Comparison between hyaluronic acid and platelet-rich plasma, intra-articular infiltration in the treatment of gonarthrosis. *The American journal of sports medicine*, 40(12), 2822–2827. <https://doi.org/10.1177/0363546512461902>
 15. Hall, M. P., Band, P. A., Meislin, R. J., Jazrawi, L. M., & Cardone, D. A (2009) Platelet-rich plasma: current concepts and application in sports medicine. *The Journal of the American Academy of Orthopaedic Surgeons*, 17(10), 602–608. <https://doi.org/10.5435/00124635-200910000-00002>
 16. Ramakrishnan DS, Kandamani J, Senthil Nathan KP (2022) Comparison of intraarticular injection of platelet-rich plasma following arthrocentesis, with sodium hyaluronate and conventional arthrocentesis for management of internal derangement of temporomandibular joint. *Natl J Maxillofac Surg*. May-Aug;13(2):254-261. doi: 10.4103/njms.NJMS_94_20. Epub 2022 Jun 15
 17. Mahmoud, N (2018) Sodium hyaluronic acid, platelet rich plasma and dextrose prolotherapy in management of Temporo-mandibular joint internal derangement. A Comparative study. *Egyptian Dental Journal*, 64(Issue 2 - April (Oral Surgery)), 1055-1069. doi: 10.21608/edj.2018.76957
 18. Nabil, Y., Seleem, H., & Hassan, N (2019) Comparative study of the use of arthrocentesis and arthrocentesis in addition with platelet rich plasma in management of temporomandibular joint internal derangement. *Egyptian Journal of Oral and Maxillofacial Surgery*, 10(1), 9-19. doi: 10.21608/omx.2019.10885.1027
 19. Attia AAMM, Awad SS (2023) Hyaluronic Acid and Platelet-Rich Plasma Mixture Versus Hyaluronic Acid and

- Corticosteroid in the Treatment of Temporomandibular Joint Internal Derangement: A Comparative Randomized Study. *J Maxillofac Oral Surg.* Apr 5;23(2):1-7. doi: 10.1007/s12663-023-01907-6. Epub ahead of print.
20. Shakil Ahmed Nagori, Venkatesan Gopalakrishnan, H. Rangarajan, Vishal Kulkarni, Ajoy Roychoudhury (2024) Does intra-articular injection of platelet-rich plasma/platelet-rich fibrin improve outcomes after temporomandibular joint arthrocentesis? A systematic review and meta-analysis, *British Journal of Oral and Maxillofacial Surgery*, 62: (8), 676-684, <https://doi.org/10.1016/j.bjoms.2024.06.007>
 21. Lee, Y. H., Lee, K. M., & Auh, Q. S (2021) MRI-Based Assessment of Masticatory Muscle Changes in TMD Patients after Whiplash Injury. *Journal of clinical medicine*, 10(7), 1404. <https://doi.org/10.3390/jcm10071404>
 22. Talmaceanu, D., Lenghel, L. M., Bolog, N., Hedesiu, M., Buduru, S., Rotar, H., Baciut, M., & Baciut, G (2018) Imaging modalities for temporomandibular joint disorders: an update. *Clujul medical* (1957), 91(3), 280–287. <https://doi.org/10.15386/cjmed-970>
 23. Mustafa G. Khallaf, Andrew J. Sidebottom, Hussien Elrawy, and Mohammed Elmasry (2019) Evaluation Of Platelet-Rich Plasma Effect on Treatment of Temporomandibular Joint Anterior Disc Displacement. *American Journal of Oral and Maxillofacial Surgery* <http://ivyunion.org/index.php/maxillofacialResearch>., 6: 14 -26
 24. Eberhard, Lydia & Giannakopoulos, Nikolaos & Rohde, Stefan & Schmitter, Marc (2013) Temporomandibular Joint (TMJ) Disc Position in Patients with TMJ Pain assessed by coronal MRI. *Dento maxillo facial radiology*. 42. 10.1259/dmfr.20120199.
 25. Kutlu B, Tıǧlı Aydın RS, Akman AC, Gümüşderelioglu M, Nohutcu RM. Platelet-rich plasma-loaded chitosan scaffolds: preparation and growth factor release kinetics. *J Biomed Mater Res B Appl Biomater*. 2013 Jan;101(1):28-35. doi: 10.1002/jbm.b.32806. Epub 2012 Sep 15. PMID: 22987323.
 26. Aniket U. Vaidya, Nivedita Chinam , Manisha M. Khorate, Nigel Figueiredo (2020). TMJ Disc Displacement Angle Analysis in MRI: A New Proposal. *Open Journal of Dentistry and Oral Medicine* (CEASE PUBLICATION), 8(2), 11 - 16. DOI: 10.13189/ojdom.2020.080201
 27. Poluha, R. L., Canales, G. T., Costa, Y. M., Grossmann, E., Bonjardim, L. R., & Conti, P. C. R (2019) Temporomandibular joint disc displacement with reduction: a review of mechanisms and clinical presentation. *Journal of applied oral science: revista FOB*, 27, e20180433. <https://doi.org/10.1590/1678-7757-2018-0433>
 28. Abbadi, W., Kara Beit, Z., & Al-Khanati, N. M (2022) Arthrocentesis, Injectable Platelet-Rich Plasma and Combination of Both Protocols of Temporomandibular Joint Disorders Management: A Single-Blinded Randomized Clinical Trial. *Cureus*, 14(11), e31396. <https://doi.org/10.7759/cureus.31396>
 29. Singh, A. K., Sharma, N. K., Kumar, P. G. N., Singh, S., Mishra, N., & Bera, R. N (2021) Evaluation of Arthrocentesis with and Without Platelet-Rich Plasma in the Management of Internal Derangement of Temporomandibular Joint: A Randomized Controlled Trial. *Journal of maxillofacial and oral surgery*, 20(2), 252–257. <https://doi.org/10.1007/s12663-019-01320-y>
 30. Hossameldin, R.H., & McCain, J.P (2017) Efficacy of platelet-rich plasma versus hyaluronic acid intraarticular injection in arthroscopic management of Wilkes V temporomandibular joint patients. *International Journal of Oral and Maxillofacial Surgery*, 46, 229-230.
 31. Lin SL, Tsai CC, Wu SL, Ko SY, Chiang WF, Yang JW (2018) Effect of arthrocentesis plus platelet-rich plasma and platelet-rich plasma alone in the treatment of temporomandibular joint osteoarthritis: a retrospective matched cohort study. *Medicine* 97(16): e477–e484
 32. A.K.M Habibullah, Md. Wares Uddin, MD (2023) Asaduzzaman, Wahidujjaman, Md. Mahmudul Hasan, Mozammel Hossain, “Evaluation of Arthrocentesis with and without Platelet Rich Plasma in the Internal Derangement of Temporomandibular Joint,” *SSRG International Journal of Medical Science*, vol. 10, no. 3, pp. 1-6, Crossref, <https://doi.org/10.14445/23939117/IJMS-V10I3P101>
 33. Ghoneim, N. I., Mansour, N. A., Elmaghraby, S. A., & Abdelsameaa, S. E (2022) Treatment of temporomandibular joint disc displacement using arthrocentesis combined with injectable platelet rich fibrin versus arthrocentesis alone. *Journal of dental sciences*, 17(1), 468–475. <https://doi.org/10.1016/j.jds.2021.07.027>
 34. Hancı, M., Karamese, M., Tosun, Z., Aktan, T. M., Duman, S., & Savaci, N (2015) Intra-articular platelet-rich plasma injection for the treatment of temporomandibular disorders and a comparison with arthrocentesis. *Journal of cranio-*

- maxillo-facial surgery: official publication of the European Association for Cranio-Maxillo-Facial Surgery, 43(1), 162–166. <https://doi.org/10.1016/j.jcms.2014.11.002>
35. Lee, S. H., & Yoon, H. J (2009) MRI findings of patients with temporomandibular joint internal derangement: before and after performance of arthrocentesis and stabilization splint. *Journal of oral and maxillofacial surgery: official journal of the American Association of Oral and Maxillofacial Surgeons*, 67(2), 314–317. <https://doi.org/10.1016/j.joms.2008.07.009>
 36. Ohnuki, T., Fukuda, M., Nakata, A., Nagai, H., Takahashi, T., Sasano, T., & Miyamoto, Y (2006) Evaluation of the position, mobility, and morphology of the disc by MRI before and after four different treatments for temporomandibular joint disorders. *Dento maxillo facial radiology*, 35(2), 103–109. <https://doi.org/10.1259/dmfr/25020275>
 37. Moses, J. J., Sartoris, D., Glass, R., Tanaka, T., & Poker, I (1989) The effect of arthroscopic surgical lysis and lavage of the superior joint space on TMJ disc position and mobility. *Journal of oral and maxillofacial surgery: official journal of the American Association of Oral and Maxillofacial Surgeons*, 47(7), 674–678. [https://doi.org/10.1016/s0278-2391\(89\)80004-7](https://doi.org/10.1016/s0278-2391(89)80004-7)