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ASSESSMENT OF INJECTABLE PLATELET-RICH FIBRIN WITH HYALURONIC ACID VERSUS HYALURONIC ACID IN MANAGEMENT OF TEMPOROMANDIBULAR JOINT INTERNAL DERANGEMENT. (A RANDOMIZED CLINICAL TRIAL)

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ABSTRACT

Objectives : To assess the effectiveness of injectable platelet rich fibrin (I-PRF) / Hyaluronic acid (HA) versus HA injection following arthrocentesis in management of TMJ internal derangement.

Materials and methods: A randomized controlled clinical trial of thirty patients with TMJ internal derangement were included according to the eligible criteria, and equally divided into three groups: arthrocentesis (Comparator 1), arthrocentesis with HA injection (Comparator 2), and arthrocentesis with HA and I-PRF injection (study). All groups were assessed clinically in terms of pain intensity (10 point -visual analogue scale/VAS). Pain score was recorded preoperatively and postoperatively (1 week, 1 month, and 3 months).

Results: There was a significant reduction in VAS scores for pain intensity across all groups over time ($p<0.001$).. However, the arthrocentesis alone group showed the most pronounced reduction in pain scores compared to the other two groups.

Conclusions: arthrocentesis is an effective treatment approach for temporomandibular joint internal derangement. The addition of HA or I-PRF+HA did not seem to provide a significant added benefit in terms of pain reduction over 3 months.

Clinical Relevance: The results suggest that arthrocentesis alone may be a sufficient treatment approach for some patients.

KEYWORDS: injectable platelet-rich fibrin, hyaluronic acid ,internal derangement, temporomandibular joint, arthrocentesis

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INTRODUCTION

Temporomandibular disorders (TMDs) are a collection of frequently painful and/or dysfunctional problems affecting the temporomandibular joint (TMJ), muscles of mastication, and related head and neck musculoskeletal structures. (Scrivani et al.,2008)

TMDs encompasses a wide range of disorders. One of the most prevalent types of TMDs is internal derangement (ID) (Emshoff, R. & Rudisch., 2007). ID is by definition a disturbance of the TMJ's internal components, Where the disk is malpositioned relative to the articular eminence of the temporal bone and the mandibular condyle. ID is described by the American Association of Oral and Maxillofacial Surgeons (AAOMS) as a change in the intracapsular components' dynamic movement that results in joint dysfunction. Typically, ID begins with a painless click with normal maximum mouth opening (MMO), advances to a painful clicking stage (disc displacement with reduction; DDWR), and finally clicking ceases and results in different levels of opening restriction (disc displacement without reduction; DDWOR).(J.P. McCain.,1996, Mehndiratta et al.,2019)

DDWR is the early stage of TMJ-ID in which the disc recaptures during mouth opening. Signs and symptoms include joint noise (clicking), pain in the TMJ region, and difficulty opening the mouth. The first sign of DDWR is a joint sound, which may or may not be accompanied by pain.

DDWOR (closed lock) is thought to result from an anteriorly misplaced, non-reducing deformed disc that blocks the sliding condylar head, making it unable to open the mouth widely.

Different types of therapy have been used to treat ID namely, Splint therapy, physical therapy, medication, and behavioral change are instances of conservative treatments. Additionally, with differing degrees of success, surgical procedures include discectomy, arthroplasty, arthrocentesis, arthroscopy, and TMJ reconstruction.(Okeson.,2003)

Regarding the intra-articular therapy of TMDs, the benefits of several injection types, including hyaluronic acid, platelet concentrates, or corticosteroids, with or without arthrocentesis, have been documented with vast degrees of heterogeneity in doses, combinations and frequency of injections on different intervals.(Karadayi & Gursoytrak., 2021)

Yet, a standard line of therapy doesn't exist for a specific ID diagnosis. Hyaluronic acid (HA) viscosupplementation is a popular modlity for treating TMD as it lowers joint surface friction, particularly when degenerative changes are present (Yilmaz et al.,2019). Numerous studies demonstrate its effectiveness in alleviating pain and increasing of motion.(Tuncel .,2012, Ferreira et al.,2018, Guarda-Nardini et al.,2014)

Among autologous blood products, one characterized by high concentrations of growth factors and biologically active chemicals is platelet-rich plasma (PRP), however, clinical outcomes depend on nuanced variables—from anticoagulant selection to activation timing—highlighting the need for protocol standardization (Magalon et al.,2016). Its second generation injectable form, injectable platelet-rich fibrin (I-PRF) was not sufficiently investigated for management of ID in literature (Choukroun & Ghanaati.,2017). Using platelet concentrates for one or more arthrocentesis procedures has demonstrated the ability to generate beneficial clinical outcomes within publications.(Işık et al.,2022)

Write paragraph about that your groups were not compared in literature or only in few studies and cite them

Thus, the intention of the current study was to assess the impact of HA versus HA/I-PRF combination following arthrocentesis on clinical pain intensity score in patients with TMJ internal derangements.

PATIENTS AND METHODS

Study design:

The current prospective, randomized clinical study was conducted at the Department of Oral and Maxillofacial (OMFS) Surgery, Faculty of dentistry of Cairo university, Egypt. This study was carried out with the approval of the institutional Ethics Committee at Cairo university, Egypt (No : 12424).

Eligibility criteria:

Patients were selected from Cairo University's Faculty of Dentistry's OMFS clinic with MRI-confirmed TMJ internal derangement (ID) presenting symptoms like pain or clicking, who had failed conservative treatment. Exclusion criteria included systemic diseases (e.g., rheumatoid arthritis), prior TMJ surgery, hypersensitivity to HA, recent use of anti-coagulants, muscle relaxants, NSAIDs (within 48 hours), or corticosteroid injections (site within one month/systemic within two weeks Ben-nafa and Munro.,2018). Eligible, Following comprehensive explanation, willing participants gave written informed consent.

Randomization and Allocation process

Patients were randomized into one of three equal study arms using a computer-generated program, with allocation concealed from the principal investigator by an assistant officer who placed the computer-generated numbers in opaque envelopes; the groups were differentiated by the arthrocentesis technique used: Group I (control) received arthrocentesis with 100 milliliters of normal saline only; Group II (HA group) received arthrocentesis with 100 mL of normal saline followed by an intra-articular injection of 1 mL of HA; and Group III (I-PRF group) received arthrocentesis with 100 mL of normal saline followed by an intra-articular injection of 1 mL of I-PRF and then a 1 mL HA injection.

Preoperative patient assessment

An extensive history and clinical examination, including measurement of maximum mouth opening (MMO), detection of joint sounds, and pain assessment via a visual analog scale (VAS), were obtained from each patient; preoperative TMJ MRI scans (T1 and T2 sequences in both open and closed joint positions) were also requested. All preoperative measurements were documented for subsequent analysis.

Intraoperative procedures

Arthrocentesis targeting the superior joint compartment was administered to all participants in the three study groups using local anesthesia*.

After aseptic preparation with Betadine** followed by 70% alcohol, auriculotemporal nerve block (Mepivacaine 2% with Levonordefrin) and local infiltration were delivered. Anatomical landmarks were followed to draw the cantho-tragal line (10mm from tragus centre and 2mm below for posterior entry; 10mm along and 10mm below the same line for anterior entry). Then, Dual 18-gauge needle insertion was performed targeting the temporomandibular joint's superior compartment. The joint was distended with ~2ml normal saline via the posterior needle, followed by irrigation with 100ml saline using two-needle technique, while mandibular manipulation enhanced adhesion lysis during lavage. Patients were then divided: For group A, patients received saline arthrocentesis only, Group B received an additional 1ml hyaluronic acid (HYALGAN®)***, and Group C received 1ml HA followed by 1ml I-PRF post-arthrocentesis (Figure 1).

* Mepecaine L: 2% with Levonordefrin 1:20000, Alexandria Co.

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

*** Hyalgan, Italy

Fig. (1) A Clinical photograph showing: a. Landmarks tracing for arthrocenthesis (Canthotragal line), b. Hyalronic acid injection into superior joint space following arthrocentesis & c.I-PRF injection.

Preparation of I-PRF

I-PRF was prepared by collecting blood (10 ml) aseptically from the antecubital vein into sterile plain 10 ml vacuum tubes without any other ingredients. The blood was immediately centrifuged (Spin plus centrifuge) at 700 rpm (60 g force) for 3 minutes. The process yielded sedimented RBCs below and liquid PRF supernatant above, with a volumetric ratio near 7:2. A maximum intake of 1 ml of the resulting i-PRF was then injected into the superior joint space in group C patients. Figure 2

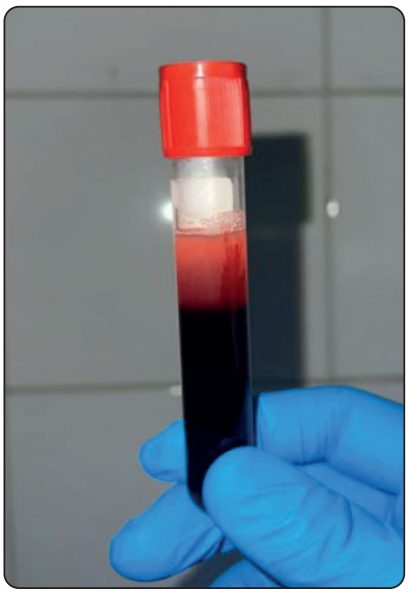

Fig. (2): I-PRF (top layer) after centrifugation of blood sample.

Post operative care and instructions

To minimize swelling and inflammation post-surgery, all patients were instructed to apply ice to the operated pre-auricular region in cycles of 10 minutes on followed by 5 minutes off for four hours and to follow a soft diet for one week. They were prescribed a regimen of one 300 mg clindamycin* tablet and one 400 mg ibuprofen** tablet and every eight hours for five days.

Clinical parameters were evaluated preoperatively and at 1 week, 1 month, and 3-month follow-ups. Patients' self-reported pain intensity, measured on a 10-point VAS, constituted the primary outcome.

Statistical analysis :

Data were presented as numbers, percentages, means, and ranges. The Kolmogorov-Smirnov test demonstrated adherence to normal distribution assumptions; consequently, parametric tests including One-way Analysis of Variance (ANOVA) and repeated measures ANOVA were employed to examine differences between related means within groups, with post-hoc comparisons performed using Bonferroni correction, all conducted at a significance level of $p \leq 0.05$ using SPSS version 23.0 for Windows.

* Dalacin® C, Pfizer co

** Brufen 400 mg, Pfizer

RESULTS

Thirty patients who were diagnosed DDWR were enrolled in the current study (28 female & 2 .male) with mean age of 28 Years

There was a significant reduction in VAS scores for pain across all groups over time (p<0.001). Specifically, each group showed a significant reduction in VAS scores at follow-up compared to the preoperative values. Furthermore, the comparison between groups at each time point revealed significant differences (p<0.001). The arthrocentesis alone group showed the most pronounced reduction in VAS scores, with a decrease from 7.10±1.20 preoperatively to 0.20±0.06 at 1 and 3 months post-operative, which was significantly different from the other two groups **(Table 1).**

TABLE (1) Comparison of VAS score (mean and SD) for each group and one way and RMANOVA test for parametric quantitative data between the three groups and time intervals followed by Bonferroni correction between each two group and each two time.

VAS score	Arthrocenthesis alone Group	Arthrocethesis + HA Group	Arthrocentesis following i-PRF +HA	p-value
Preoperative	7.10±1.20Aa	6.90±1.60Aa	7.70±1.25Aa	0.404
After 1Week	1.50±0.47Bb	5.00±1.16Ba	5.30±1.42Ba	<0.001*
After 1months	0.20±0.06Cb	4.33±1.22Ca	4.40±1.26Ca	<0.001*
After 3months	0.20±0.06Cb	3.33±0.95Da	3.70±0.67Da	<0.001*
p-value	**<0.001***	**<0.001***	**<0.001***	

SD: Standard deviation; Significance level p≤0.05 , *significant

Bonferroni correction for multiple comparisons

Different capital letters indicate significant difference at (p<0.05) among means in the same column

Different small letters indicate significant difference at (p<0.05) among means in the same row

****Significant Different.***

DISCUSSION

Internal derangement (ID) of temporomandibular joint (TMJ) represents a spectrum of biomechanical disorders that is marked by unconventional positioning of the disc relative to the condyle and eminence. It affects 5-12% of the population, predominantly women aged 20-40 years, manifesting as pain, joint sounds, restricted mandibular mobility, and diminished quality of life (Yuce & Komerik.,2020, Ramakrishnan et al.,2022).

Current management strategies range from conservative approaches to minimally invasive procedures such as arthrocentesis—a joint lavage technique that removes inflammatory mediators and lyses adhesions. While arthrocentesis alone provides symptomatic relief, its efficacy is often enhanced by intra-articular injections of viscoelastic supplements like HA or bioactive agents like I-PRF. (Yuce & Komerik (2020), Dasukil et al.,2022)

Furthermore, the therapeutic synergy between HA and i-PRF is unexplored despite network meta-analyses suggesting superior short-term outcomes

for HA combined with PRP and evidence that i-PRF outperforms HA in long-term pain reduction and functional improvement at 9–12 months (Yuce & Komerik (2020), yet no clinical trials directly evaluate HA+i-PRF combinations, creating uncertainty about potential additive or synergistic benefits (Uysa et al.,2024).

The particular intention of the current research was to compare the effectiveness of arthrocentesis versus arthrocentesis with intra-articular injection of hyaluronic acid with or without I-PRF .

The results of the study was that all three treatment groups showed significant reductions in pain scores over time. However, arthrocentesis alone yielded the most reduction of pain scores compared to the other two groups.

Arthrocentesis is an efficient therapeutic option for TMJ disorders (Nitzan et al.,1991, Alhoor et al.,2025). In order for arthrocentesis to be effective, it should improve jaw movement by reducing negative intra-articular pressure through the elimination of adhesions and rehabilitation of the characteristics of joint fluid. Moreover, it should reduce pain by eliminating chemical mediators of inflammation, degenerative products, and enzymes responsible for wearing off joints (Yuce & Komerik (2020), Hegab et al.,2015). Intra-articular injection of several adjunctive medicines has been researched for better outcomes regardless of arthrocentesis efficacy (Aktas et al.,2010, Ishimaru et al.,2003).

Hyaluronic acid, a core component of synovial fluid, provides viscoelastic lubrication and shock absorption. In TMJ inflammatory conditions, the inflammation degrades endogenous HA into low-molecular-weight fragments, increasing friction and promoting cartilage degradation. Exogenous HA injections restore synovial fluid rheology by replenishing high-molecular-weight HA to rebuild the entangled molecular network, thereby reinstating viscous lubrication and elastic cushioning properties, suppress pro-inflammatory cytokines, and inhibit matrix metalloproteinases (MMPs), thereby mitigating pain and improving joint mobility (Yuce & Komerik.,2020, Tepecik & Gedik., 2025).

Injectable platelet-rich fibrin (i-PRF), an autologous platelet concentrate, that is prepared and utilized to preserve leukocytes, representative growth mediators. It exerts anti-inflammatory effects by reducing IL-6 and prostaglandin E2, promotes angiogenesis and chondrogenesis, and enables sustained growth factor release over 7–28 days. Combining i-PRF with HA creates a synergistic effect, HA provides immediate biomechanical support, while i-PRF enhances tissue regeneration and modulates inflammatory factors (Ramakrishnan et al.,2022 , Xu et al.,2023). I-PRF protocols for temporomandibular joint (TMJ) disorders typically involve the centrifugation of 10–20 mL of autologous peripheral blood at 700 rpm for 3 minutes without anticoagulants to produce a liquid platelet concentrate rich in leukocytes, platelets, and growth factors (Kumar et al.,2024, Kumar et al.,2025). I-PRF is then injected into the superior joint space (1–2 mL per joint) using an anatomical landmark approach (approximately 10 mm anterior to the tragus and 2 mm below the canthotragal line), often following arthrocentesis irrigation (Kumar et al.,2024, Kumar et al.,2025).

Guarda-Nardini et al.,2012 and Manfredini et al., 2009 documentd improvements in discomfort, functional impairment, and MMO after arthrocentesis with multiple injections of HA which were delivered across 5 weeks with sequential follow-ups at 3 and 6 months post-treatment.

Bouloux et al.,2017 investigated early-phase outcomes of HA administration post-arthrocentesis and discovered that single intra-articular HA injection after arthrocentesis does not demonstrate the added therapeutic value in symptom reduction and functional enhancement at 1 and 3 months post-treatment compared to isolated arthrocentesis.

Few published studies have appraise the thera-

peutic effectiveness of I-PRF injections in TMJ or extra-articular synovial joints (Albilia et al.,2020, Abd El Raouf et al.,2019). Research indicates injectable PRF exerts therapeutic effects through hydraulic adhesiolysis: eliminating joint negative pressure, recovering optimal lubricant viscosity in articular fluid, and improving intracapsular blood flow by sustained secretion of bioactive factors. (Albilia et al.,2020, Abd El Raouf et al.,2019).

Albilia et al.,2020, among 37 patients with TMJ dysfunction (47 affected joints), 69% achieved clinically significant pain and functional improvements sustained through 12-month follow-up after i-PRF therapy. Also Ghoneim et al.,2021 report a statistically significant reduction in pain intensity was documented at 6 months postoperatively when I-PRF was administered after arthrocentesis..

Yuce & Komerik 2020., reported that I-PRF utilization has yielded more notable reductions in mouth opening restriction and TMJ-ID-related pain compared to arthrocentesis plus HA injection and arthrocentesis monotherapy (control), aligning with Albilia et al.'s 2020 results. However, these results contradict our own results over a 3-month period.

The current study's primary limitation was its dependence on a relatively small population. Moreover, the present study was designed to compare the clinical outcomes of intra-articular single injection of HA with or without I-PRF and the other investigetor had a multi-injections regimens of I-PRF or HA for TMJ ID. In addition to i-PRF's efficacy depends on centrifugation protocols and injection volume, The centrifugation protocols for I-PRF significantly influence its biological composition and therapeutic efficacy when used in temporomandibular joint (TMJ) intra-articular injections. Standardized preparation typically involves centrifuging venous blood at low relative centrifugal forces (RCF) of approximately 60-70 g (equivalent to 700 rpm) for short durations of 3 minutes, which optimizes the cellular content by preserving higher concentrations of platelets, growth factors, and leukocytes critical for tissue regeneration and anti-inflammatory modulation (Kumar et al.,2024, Işık et al.,2022). This protocol minimizes erythrocyte contamination and prevents premature fibrin polymerization, ensuring a liquid formulation suitable for injection while maintaining bioactivity (Işık et al.,2022, Herrera-Vizcaino & Albilia.,2021). Deviations from these parameters—such as increased speed or prolonged centrifugation—risk depleting leukocyte populations and altering the release kinetics of growth factors like VEGF, TGF-β, and PDGF, thereby reducing I-PRF's regenerative potential (Herrera-Vizcaino & Albilia.,2021, Chęciński et al.,2023). Furthermore HA molecular weight also affects durability, with high-weight formulations providing longer-lasting effects and our result based on low-weight formula of HA.

CONCLUSION

The results suggest that all three treatments are effective in reducing pain, but the arthrocentesis alone group showed the most significant improvement.

RECOMMENDATIONS

Confirmatory studies are warranted to verify these results and define evidence-based treatment parameters for temporomandibular joint internal derangement. Future studies should investigate the long-term outcomes, potential complications of arthrocentesis and adjunctive treatments for temporomandibular joint internal derangement.

Conflict of interest

Authors declare no conflict of interest

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