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Injectable Platelet-Rich Fibrin With or Without Hyaluronic Acid After Arthrocentesis for Temporomandibular Joint Internal Derangement: A Randomised Controlled Trial

Manoj K Malya
Vishnu Dental College
Divya Puvvada
puvvadadivya87@gmail.com

Vishnu Dental College
Uddarraju Shivaji Raju
Vishnu Dental College
Kishore Moturi
Army College Of Dental Sciences
Pampana Sravani
Vishnu Dental College
Siva Dilip Sami
Vishnu Dental College

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Abstract

Purpose

To compare six-month clinical outcomes of arthrocentesis alone with arthrocentesis plus injectable platelet-rich fibrin (I-PRF), hyaluronic acid (HA), or both (I-PRF + HA) in Wilkes stage II–III temporomandibular joint (TMJ) internal derangement.

Methods

In this prospective four-arm randomised trial, 56 patients with unilateral TMJ internal derangement (14 per group) were followed for six months. The primary outcome was pain intensity (visual analogue scale, VAS). Secondary outcomes were mandibular range of motion, quality of life (Oral Health Impact Profile-14, OHIP-14) and rescue analgesic use. Masticatory efficiency and ultrasound-assessed disc position were exploratory.

Results

At six months, mean VAS in the I-PRF + HA group fell from 7.5 to 1.9, compared with 4.2 after arthrocentesis alone ($p < 0.001$ across groups). Maximum mouth opening reached 43.6 ± 2.5 mm in the combination group versus 36.3 ± 2.9 mm after arthrocentesis alone ($p < 0.001$). OHIP-14 improved by 12.8 points in the combination group. Rescue analgesic use was lowest with the combination (1.8 ± 0.89 tablets), significantly lower than with arthrocentesis alone or HA alone ($p < 0.01$) but not than with I-PRF alone ($p = 0.07$). The I-PRF and I-PRF + HA groups did not differ significantly at later time points.

Conclusion

In this small trial, I-PRF-containing regimens, particularly I-PRF + HA, were associated with greater improvements in pain and function than arthrocentesis alone or with HA alone. The added benefit of HA over I-PRF alone was not demonstrated. These preliminary findings require confirmation in larger, adequately powered trials.

Trial registration:

CTRI/2023/11/059991, registered 20/11/2023.

Introduction

Internal derangements of the temporomandibular joint (TMJ), abbreviated here as TMJ-ID, are a progressive condition in which there is impaired coordination and disruption of the disc-condyle alignment [1]. Disc displacement, the hallmark of TMJ-ID, is among the most prevalent joint disorders, with a pooled prevalence of about 19% in adult general populations [2] and about 41% of diagnoses among patients with temporomandibular disorders (TMD) in clinical samples [3]. It manifests as pain, clicking and impaired jaw mobility [4], and negatively affects daily quality of life. These symptoms, if left unattended, could result in more progressive degenerative changes. Although a single definitive aetiology cannot be identified in all cases, the factors contributing to the development and progression of TMJ internal derangement can generally be categorised as: a normal joint exposed to excessive load from macrotrauma or microtrauma, or an abnormal joint exposed to normal functional load, as seen in conditions such as rheumatoid arthritis, systemic lupus erythematosus, psoriatic arthritis, or synovial chondromatosis [5, 6].

Conservative management—such as splints, physiotherapy, pharmacologic agents, and photobiomodulation remains the cornerstone of initial therapy [7]. However, a notable subset of patients fail to respond or do not achieve lasting relief, necessitating minimally invasive interventions. Arthrocentesis, introduced as a straightforward lavage technique, has demonstrated the ability to flush inflammatory mediators, break adhesions, and restore smoother disc–condyle movement [8]. Its simplicity and favourable safety profile have made it an appealing option in moderate functional limitation, though repeated arthrocentesis may be required depending on severity.

The search for improved, longer-lasting outcomes has led to the adjunctive use of intra-articular biologics. Hyaluronic acid (HA) is a naturally occurring elastoviscous biopolymer synthesised by chondrocytes and synovial cells, essential for maintaining joint lubrication and cushioning against impact [9]. Intra-articular viscosupplementation with HA injections for TMJ-ID has been shown to restore synovial fluid characteristics and provide symptomatic relief, but the effect is short-lived and often requires repeated injections [10, 11].

Blood-derived concentrates are gaining popularity for arthrogenous disorders of the knee and TMJ. Platelet-rich plasma (PRP), a first-generation autologous concentrate, stimulates glycosaminoglycan synthesis, angiogenesis, and cartilage regeneration [12, 13]. Platelet-rich fibrin (PRF), a second-generation concentrate, offers a stronger fibrin matrix and higher growth-factor concentration than PRP without needing anticoagulants. Injectable PRF (I-PRF), a liquid form produced by low-speed centrifugation, promotes fibroblastic migration and the expression of growth factors such as platelet-derived growth factor (PDGF) and transforming growth factor-β (TGF-β) and of collagen I, and is easier to inject into joint spaces, enabling even distribution within the joint space [14, 15].

In orthopaedics, combining platelet concentrates with HA in degenerative knee disease has shown greater improvements in pain and function than either agent alone [16, 17]. Despite this evidence, similar combination protocols remain largely unexplored in TMJ-ID management, and comparative studies in maxillofacial literature are scarce. It can be hypothesised that combining I-PRF and HA after

arthrocentesis will achieve greater and more sustained improvements in pain, mandibular function, and patient-reported quality of life compared to either treatment alone or arthrocentesis alone. This study aimed to evaluate and compare the clinical outcomes of arthrocentesis alone, arthrocentesis with I-PRF, arthrocentesis with HA, and arthrocentesis with an I-PRF + HA combination in patients with Wilkes Stage II–III TMJ internal derangements over a 6-month follow-up period.

Materials and Methods

This prospective, randomised clinical trial was conducted at Vishnu Dental College, Andhra Pradesh, India, between November 2023 and August 2025, after obtaining approval from the Institutional Ethics Committee (IECVDC/23/PG01/OMFS/IVV/30). Written informed consent was obtained from all participants. The trial was registered with the Clinical Trials Registry – India (CTRI), registration number CTRI/2023/11/059991, registered 20/11/2023. Participant enrolment began only after ethics approval and trial registration. The study was reported in accordance with the Consolidated Standards of Reporting Trials (CONSORT) 2010 statement.

Fifty-six patients aged 18–40 years with unilateral TMJ internal derangement (Wilkes Stage II or III; maximum mouth opening < 35 mm), confirmed by clinical examination and ultrasonography, were recruited (Fig. 1).

Eligible participants were adults aged 18–40 years with unilateral TMJ internal derangement (Wilkes Stage II or III), refractory to conservative management for ≥ 6 weeks, including non-steroidal anti-inflammatory drugs (NSAIDs), occlusal splints, and physiotherapy, willing to give consent and comply with the 6-month follow-up. Exclusion criteria were significant systemic or malignant disease, previous TMJ surgery or condylar trauma, technical failure of intra-articular access, TMJ ankylosis (fibrous or bony), local infection involving the auricular, cutaneous, or intra-articular region, edentulous status, pregnancy or lactation, and known hypersensitivity to hyaluronic acid.

Sample Size Calculation

Sample size (n = 14 per group) was calculated using G*Power version 3.1, with pain intensity measured by the visual analogue scale (VAS) at 6 months specified as the primary outcome. The calculation assumed a repeated-measures analysis of variance (ANOVA), with an effect size of f = 0.35, α = 0.05, 80% power, a correlation among repeated measures of 0.5, and a nonsphericity correction of 1.0. The selected effect size corresponded approximately to a between-group mean difference of 2.0 points on the 0–10 pain scale, an assumed clinically relevant difference that is broadly in line with minimal clinically important differences reported for pain intensity in chronic temporomandibular disorders [18], although those estimates were not specific to the VAS. The calculation was not designed for pairwise comparisons between the four groups or for testing an I-PRF × HA interaction, so the study is best regarded as exploratory. Allowing for a 10% potential dropout, a total of 56 patients were recruited and equally allocated to the four groups.

Randomisation and Allocation Concealment

Participants were randomly allocated into four groups (n = 14 per group) using a computer-generated block randomisation method (block size = 4) to ensure balanced distribution across groups. The randomisation sequence was generated by an independent investigator who had no role in participant enrolment, treatment, or outcome assessment. Allocation concealment was maintained using sequentially numbered, opaque, sealed envelopes prepared in advance. The study coordinator revealed the allocation to the operating surgeon after enrolment and completion of baseline assessment.

Blinding

Due to the nature of the interventions, neither participants nor treating clinicians could be blinded. However, postoperative outcome assessment was performed by a single calibrated evaluator who was blinded to group allocation and remained blinded throughout the study period. The assessor had no involvement in participant enrolment, randomisation, or treatment delivery, thereby reducing the potential for detection bias.

Study Groups

Each participant underwent standard two-needle arthrocentesis using 100–150 mL of Ringer's lactate. Post-lavage, intra-articular injections were administered as follows

Group I

Arthrocentesis only

Group II

Arthrocentesis + injectable platelet-rich fibrin (I-PRF)

Group III

Arthrocentesis + hyaluronic acid (HA)

Group IV

Arthrocentesis + combination of I-PRF and HA

Preparation of I-PRF and HA Combination

I-PRF was prepared using an automated horizontal centrifuge (SHK Hexad, Delhi, India). Twenty millilitres of venous blood was collected in two sterile, non-coated plastic tubes supplied by the manufacturer and processed using the dedicated i-PRF program (equivalent to ~ 700 rpm; ≈60 g for 3 minutes), which

automatically completes the preparation [14]. The upper liquid I-PRF fraction was immediately aspirated within 90 seconds of centrifugation into a 2 mL sterile single-use disposable syringe (Dispovan 2 mL Syringe with 23G Needle) to maintain its injectable consistency and was injected within 10 minutes (Supplementary Information, Online Resource 1).

Commercially available hyaluronic acid (Hyalgan®, 20 mg/2 mL; FIDIA Pharma, Online Resource 1) was added to I-PRF in a 1:2 ratio (0.5 mL HA: 1 mL I-PRF) into the same syringe to create a homogenised solution. The components were gently mixed to obtain a homogeneous injectable preparation and administered within 10 minutes.

Surgical Procedure

All patients underwent standard two-needle arthrocentesis as per the technique developed by Nitzan et al. in 1991 [8]. 2% lignocaine with 1:200,000 adrenaline was used to deposit an Auriculo-temporal nerve block. Two 21-G needles (Dispovan 21-G, 38 mm long needle) were used to gain entry into the superior joint compartment. The joint space was lavaged with 100–150 mL of Ringer's lactate [19] (Online Resource 1). Following lavage:

- Group I received no additional injection
- Group II received 1.0 mL I-PRF
- Group III received 0.5 mL HA
- Group IV received 1.5 mL of HA + I-PRF homogenate

Injections were administered into the superior joint space, using the first entry needle as the injection port (Online Resource 1). The second port needle was removed prior to injection, and gentle external pressure with sterile gauze was applied to minimise leakage. Patients were advised to follow a soft diet, take NSAIDs as a rescue analgesic (ibuprofen 400 mg whenever necessary for 7 days), and do jaw physiotherapy after surgery.

Outcome Measures

Primary Outcome

Pain intensity, measured using a 10-cm Visual Analogue Scale (0 = no pain, 10 = worst pain imaginable).

Secondary Outcomes:

1. Mandibular range of motion (ROM) – maximum interincisal opening (MIO) in mm (digital Vernier caliper, maximum pain-free opening); lateral excursion reported as the mean of right and left measurements (Online Resource 1).
2. Oral health-related quality of life – Oral Health Impact Profile-14 (OHIP-14; 14 items, 0–4 each; total 0–56; lower = better).

3. Rescue analgesic consumption – Ibuprofen 400 mg tablets consumed in the first 7 days post-procedure (patient diary).
4. Joint sounds and muscle tenderness – joint clicking (presence/absence, assessed according to the Diagnostic Criteria for Temporomandibular Disorders, DC/TMD) and muscle tenderness (0–3 graded, 1 kg algometer, DC/TMD), reported as one clinical-signs domain.

Exploratory Outcomes:

1. Masticatory efficiency – patient-reported ability to chew 8 representative foods, each scored 1–5 (total 8–40; higher = better). Instrument not independently validated; results are hypothesis-generating.
2. Ultrasound-based disc-condyle position – high-frequency (≥ 10 MHz) ultrasound at baseline and 6 months, interpreted by a blinded radiologist.

Masticatory efficiency and ultrasound-based disc-condyle position were treated as exploratory outcomes because of limitations in independent validation of the masticatory-efficiency instrument and the limited structural inference possible from ultrasound assessment.

Follow-Up and Assessment Timeline

All prespecified clinical parameters were assessed at the following time points:

1. Baseline: VAS, ROM, joint clicking, muscle tenderness, masticatory efficiency, OHIP-14, and ultrasound-based disc-condyle position
2. 1 week: VAS, ROM, joint clicking, and rescue analgesic consumption
3. 1 month: VAS, ROM, joint clicking, and muscle tenderness
4. 3 months: VAS, ROM, joint clicking, OHIP-14, and masticatory efficiency
5. 6 months: VAS, ROM, joint clicking, muscle tenderness, masticatory efficiency, OHIP-14, and ultrasound-based disc-condyle position

Statistical Analysis

Data are presented as mean ± standard deviation (SD) or n (%). Between-group differences in continuous outcomes at each time point were compared using one-way ANOVA with Bonferroni post hoc tests, and categorical variables using the chi-square test. Given the small sample (n = 14 per group), no covariate-adjusted or multivariable models were fitted, and all findings should be regarded as descriptive and exploratory. Statistical significance was set at $p < 0.05$. All analyses were performed using SPSS version 21.

Secondary outcomes were analysed to characterise the clinical profile of treatment response and were not individually powered. Masticatory efficiency and ultrasound-based disc-condyle position were treated

as exploratory outcomes because of limitations in measurement validation and the limited inferential value of these measures at the available sample size.

Results

A total of 56 patients, each with unilateral TMJ internal derangement, were enrolled and completed the study through all five assessment intervals: baseline, 1 week, 1 month, 3 months, and 6 months, with no dropouts recorded. Complete retention was supported by close telephone follow-up and active recall of participants, most of whom were symptomatic at enrolment and therefore motivated to report their progress; only patients able to commit to the full 6-month protocol were enrolled (see eligibility criteria). The mean age of participants was 29.9 ± 7.8 years, and 67.9% were male. Baseline demographic and clinical characteristics are summarised by group in Table 1. The distribution of Wilkes staging was 54% Stage II and 46% Stage III.

Table 1
Baseline descriptive characteristics (N = 56)

Variable	Overall(N = 56)	GroupI (n = 14)	GroupII (n = 14)	GroupIII (n = 14)	Group IV (n = 14)
Age (years), mean ± SD	29.9 ± 7.8	30.1 ± 7.5	29.6 ± 8.0	30.3 ± 7.9	29.6 ± 8.0
Sex — male, n (%)	38 (67.9%)	10 (71.4%)	9 (64.3%)	9 (64.3%)	10 (71.4%)
Wilkes stage II / III, n (%)	30 (53.6%) / 26 (46.4%)	8 (57.1%) / 6 (42.9%)	7 (50.0%) / 7 (50.0%)	8 (57.1%) / 6 (42.9%)	7 (50.0%) / 7 (50.0%)
Baseline VAS, mean	7.5 ± 1.3	7.5 ± 1.45	7.6 ± 1.40	7.4 ± 1.01	7.5 ± 1.45
Baseline MIO (mm), mean ± SD	31.6 ± 3.2	31.2 ± 3.1	31.5 ± 3.4	31.7 ± 3.2	31.8 ± 3.3
Baseline right excursion (mm)	6.33 ± 1.1	6.2 ± 1.1	6.3 ± 1.0	6.4 ± 1.2	6.4 ± 1.1
Baseline left excursion (mm)	6.23 ± 1.1	6.1 ± 1.2	6.2 ± 1.0	6.3 ± 1.1	6.3 ± 1.0
Baseline OHIP-14 (mean)	24.2 ± 1.7	24.0 ± 1.62	25.0 ± 1.75	23.5 ± 1.83	24.2 ± 1.53
Baseline masticatory score (8–40)	22.2 ± 2.3	22.3 ± 2.02	22.1 ± 1.64	22.5 ± 2.53	22.0 ± 2.91

Values are mean ± SD or n (%).

Pain Intensity (VAS Scores Over Time)

Mean VAS scores fell in all groups over follow-up, with the most pronounced reductions in Group II and Group IV. By 6 months, Group IV showed the lowest mean VAS (1.9), compared with Group I (4.2) and Group III (3.8) (overall between-group $p < 0.001$, Table 2). Group III (HA alone) showed early relief at 1 week, followed by plateauing at 3–6 months.

Bonferroni Post-hoc analysis revealed that from 1 month onward, Group IV statistically differs from Group I and Group III ($p < 0.01$). Group II and Group IV are similar at later timepoints ($p \sim 0.07–0.12$).

Table 2
VAS scores by treatment group (mean) and between-group p-values

Time point	Group I	Group II	Group III	Group IV	ANOVA p-value
Baseline	7.5 ± 1.45	7.6 ± 1.40	7.4 ± 1.01	7.5 ± 1.45	
1 week	6.2 ± 1.19	4.3 ± 1.49	4.0 ± 1.30	3.8 ± 1.19	0.002*
1 month	5.5 ± 1.45	3.0 ± 1.30	3.7 ± 1.14	2.7 ± 1.14	< 0.001*
3 months	4.6 ± 1.22	2.5 ± 1.09	3.6 ± 1.02	2.2 ± 0.80	< 0.001*
6 months	4.2 ± 1.37	2.1 ± 1.00	3.8 ± 1.19	1.9 ± 1.07	< 0.001*

Foot notes

* P < 0.05 considered statistically significant

Mandibular Range of Motion (ROM in mm)

The mean preoperative mouth opening (MIO) across all groups was 31.6 mm ± 3.2 (pooled mean ± SD), with a pooled baseline mean lateral excursion (mean of right and left) of 6.28 ± 1.1 mm. ROM improved in all groups across the study period. Group IV consistently demonstrated the highest increase in ROM, with statistically significant differences from Group I and III by 3 and 6 months ($p < 0.01$).

MIO and lateral excursions improved from baseline to 6 months in all groups (Table 3). Group IV (arthrocentesis + I-PRF + HA) consistently achieved the largest improvements at each time point. Clinically meaningful changes (≥ 2–3 mm for MIO and ≥ 1 mm for excursions) were already evident by 1 week in Groups II–IV and sustained through 6 months.

Table 3
Mandibular Range of Motion – MIO and Lateral Excursion (mean of right and left) at Each Time Point

MIO (mm)	Time Point	Arthro	Arthro + I-PRF	Arthro + HA	Arthro + I-PRF + HA	p-value (Between Groups)
	Baseline	31.2 ± 3.1	31.5 ± 3.4	31.7 ± 3.2	31.8 ± 3.3	
	1 Week	34.0 ± 3.0	36.8 ± 2.9	35.5 ± 2.8	38.4 ± 2.6	< 0.001*
	1 Month	35.2 ± 2.9	38.9 ± 2.7	37.0 ± 2.6	41.0 ± 2.4	< 0.001*
	3 Months	36.1 ± 2.8	39.7 ± 2.5	37.9 ± 2.6	42.5 ± 2.3	< 0.001*
	6 Months	36.3 ± 2.9	40.5 ± 2.7	37.8 ± 2.8	43.6 ± 2.5	< 0.001*
Lateral Excursion (mean of R + L)	Baseline	6.15 ± 1.15	6.25 ± 1.0	6.35 ± 1.15	6.35 ± 1.05	
	1 Week	7.05 ± 1.0	8.35 ± 0.9	7.75 ± 0.9	8.95 ± 0.8	< 0.001*
	1 Month	7.45 ± 1.0	8.95 ± 0.8	8.25 ± 0.9	9.75 ± 0.8	< 0.001*
	3 Months	7.75 ± 0.9	9.25 ± 0.8	8.5 ± 0.8	10.25 ± 0.7	< 0.001*
	6 Months	7.75 ± 1.05	9.55 ± 0.85	8.45 ± 1.05	10.75 ± 0.8	< 0.001*

Foot notes

* P < 0.05 considered statistically significant. Arthro, arthrocentesis; I-PRF, injectable platelet-rich fibrin; HA, hyaluronic acid; MIO, maximum interincisal opening.

Note

lateral excursion is reported as a single combined outcome (mean of separately measured right and left excursion) to reduce the number of outcome comparisons; the mean and SD shown are computed by averaging the corresponding right- and left-side summary statistics and are not derived from paired raw values.

Oral Health Impact (OHIP-14 Scores)

OHIP-14 scores improved in all groups, particularly in Groups II and IV (Table 4). The greatest improvement was observed in Group IV (Δ: 12.8 points at 6 months), indicating better perceived oral

health.

Table 4
OHIP-14 Scores Over Time (0–56, Lower = Better)

Time Point	Arthro	Arthro + I-PRF	Arthro + HA	Arthro + I-PRF + HA	p-value (between-group, ANOVA)
Baseline	24.0 ± 1.62	25.0 ± 1.75	23.5 ± 1.83	24.2 ± 1.53	
3 Months	21.1 ± 1.73	15.6 ± 1.65	19.4 ± 1.65	14.2 ± 1.53	< 0.05*
6 Months	18.7 ± 1.20	12.3 ± 1.49	16.8 ± 1.63	11.4 ± 1.50	< 0.01*

Foot notes

* P < 0.05 considered statistically significant. Arthro, arthrocentesis; I-PRF, injectable platelet-rich fibrin; HA, hyaluronic acid; OHIP-14, Oral Health Impact Profile-14.

Note

all mean and SD values in this table were recalculated from and verified against per-patient raw data.

Exploratory Outcome: Masticatory Efficiency

As this outcome used an unvalidated instrument and was not included in the primary power calculation, results are reported descriptively and should be interpreted as hypothesis-generating only. Masticatory efficiency scores improved progressively, with Group IV showing the highest improvement (from 22.0 to 35.4, $p < 0.01$) (Online Resource 2). Group II also demonstrated strong improvement.

Intergroup comparisons revealed that at 6 months, Group IV (Arthro + I-PRF + HA) had significantly higher masticatory efficiency and improved OHIP-14 scores compared with Group I (Arthro alone) and Group III (Arthro + HA). Group II (Arthro + I-PRF) also outperformed Group I and Group III. No significant difference was observed between Groups II and IV, suggesting I-PRF is the main driver of improvement, with HA providing an additive but not statistically distinct effect

Rescue Analgesic Consumption

Mean ibuprofen tablet consumption in the first 7 days was lowest in Group IV (1.8 ± 0.89) and Group II (2.1 ± 1.00), compared with 5.2 ± 1.42 in Group I and 4.0 ± 1.30 in Group III (Table 5). Group IV used significantly fewer tablets than Groups I and III ($p < 0.01$) and not significantly fewer than Group II ($p = 0.07$). Group IV was used as the reference category for these comparisons.

Table 5
Rescue Analgesic consumption

Group	Mean ± SD Tablets	*p*-value vs Group IV
Arthrocentesis only	5.2 ± 1.42	< 0.01*
Arthro + I-PRF	2.1 ± 1.00	0.07 (NS)
Arthro + HA	4.0 ± 1.3	< 0.01*
Arthro + I-PRF + HA	1.8 ± 0.89	

Foot notes

* P < 0.05 considered statistically significant. Arthro, arthrocentesis; I-PRF, injectable platelet-rich fibrin; HA, hyaluronic acid; NS, not significant.

Joint Clicking and Muscle Tenderness

A reduction in joint clicking was observed across all groups, with Group IV showing the highest rate of complete resolution (78.6%) by 6 months ($p < 0.05$). However, 2 patients (14.3%) in Group IV experienced a mild recurrence of clicking at the 6-month follow-up after achieving full resolution at 3 months.

Similarly, muscle tenderness scores, graded 0–3 using the DC/TMD palpation protocol (1 kg digital pressure), declined in Groups II and IV over time. Only 1 patient (7.1%) in Group IV reported localised tenderness recurrence at 6 months, at a lower intensity than baseline.

Exploratory Outcome: Disc Position (Ultrasound)

This exploratory imaging outcome was not included in the primary power calculation and is reported descriptively. No statistically significant changes in disc-condyle relationship were seen on ultrasound across groups between baseline and 6 months ($p > 0.1$), suggesting that structural repositioning may not underlie the functional improvements.

Discussion

TMJ-ID is a common cause of jaw pain and functional limitation. Disc displacement, with or without reduction, is among its most frequent forms, with a pooled prevalence of about 19% in adult general populations [2] and about 41% among patients with TMD in clinical samples [3]. These patterns highlight the need for minimally invasive treatments that reduce pain and restore mandibular function.

We hypothesised that combining I-PRF with HA after arthrocentesis would yield greater improvement than either agent alone. Group IV showed the most consistent improvements across pain (VAS), mandibular range of motion, patient-reported quality of life (OHIP-14) and, as an exploratory outcome,

masticatory efficiency; mean VAS fell by about 75% (from 7.5 to 1.9) by 6 months. Differences from lavage alone and HA alone were statistically significant for most outcomes, whereas the difference from I-PRF alone (Group II) was small and not statistically significant at later time points. These findings are directionally consistent with Işık et al. [20], who reported better outcomes when I-PRF was combined with arthrocentesis, but they should be interpreted cautiously given the small sample. One possible explanation is that HA provides early biomechanical lubrication while I-PRF supports longer-term regenerative processes, although this was not tested in the present trial.

I-PRF delivers a sustained release of autologous growth factors—such as PDGF, TGF-β and vascular endothelial growth factor (VEGF)—that promote angiogenesis, fibroblast proliferation, and extracellular matrix remodelling within the synovial environment. This regenerative milieu may enhance synovial membrane repair and modulate inflammatory pathways, explaining the early and sustained improvements in pain and mandibular mobility observed in our Group II. In a randomised trial, Nasef M et al. [21] reported comparable trends, with significant reductions in VAS scores and gains in maximum mouth opening persisting up to 12 months. Similarly, Torul D et al. [22] found superior clinical outcomes in Wilkes Stage III cases when I-PRF was used in conjunction with arthrocentesis compared to HA or lavage alone.

HA, beyond its viscoelastic lubricating role, also has anti-inflammatory effects, but alone after arthrocentesis, its benefit was modest and transient in Group III, corroborated by Mao et al. [23] likely reflecting limited capacity to directly stimulate regenerative repair.

The rationale for combining I-PRF with HA(Group IV) merges HA's biomechanical cushioning with I-PRF's reparative potential: HA reduces mechanical stress while I-PRF promotes synovial healing and chondrocyte viability, mirroring orthopaedic literature where intra-articular PRP/PRF combined with HA outperforms either agent alone in knee osteoarthritis [24]. In our study, this translated to the greatest and most durable improvements in VAS, ROM, OHIP-14, and masticatory efficiency, with pain reduction exceeding 70% and chewing performance improving by over 60% from baseline.

A systematic review by Xu et al. [25] similarly found that while PRP controlled pain effectively at 6–12 months, PRF improved both mouth opening and pain, making it the more effective of the two.

The improvements in patient-reported quality of life (OHIP-14) also reflect the broader functional impact of dual-agent therapy. Multi-modal biologic interventions address both the source of nociception (inflamed synovium, mechanical friction) and the consequences (muscle spasm, altered mandibular kinematics), producing changes that patients perceive as meaningful in their daily activities. This is consistent with the observation by Manafikhi et al. [26] that biologic-augmented arthrocentesis yields higher patient satisfaction than single-modality lavage.

Our data on joint clicking and muscle tenderness add nuance to the understanding of functional recovery. The majority of patients achieved complete resolution of clicking within 3 months, with sustained benefit in 78.6% of Group IV at 6 months. The small recurrence (14.3%) may be attributable to

persistent disc displacement or adaptive but incomplete remodelling of retrodiscal tissues. Muscle tenderness resolution was similarly high (92.9%), likely reflecting residual myofascial or parafunctional factors rather than joint-driven pain.

Mechanistically, these patterns may be explained by a two-phase recovery: early reduction in intra-articular inflammation improving joint biomechanics, followed by neuromuscular adaptation as reduced nociception allows masticatory muscles to normalise, lowering tenderness and improving chewing efficiency.

Strengths include the randomised design, standardised outcome measures, and multi-time-point assessment capturing both early and sustained effects, with rescue analgesic tracking as a pragmatic measure beyond subjective scales.

This trial used high-frequency ultrasonography rather than magnetic resonance imaging (MRI) to confirm eligibility and assess disc position, a deliberate trade-off reflecting resource constraints at this rural tertiary-care institution, where research MRI access is limited and costly for patients. Ultrasonography offers real-time, radiation-free, low-cost, repeatable assessment, and pooled diagnostic-accuracy data indicate clinically acceptable sensitivity and specificity for disc displacement relative to MRI [19, 27], though accuracy for non-anterior displacements and fine disc morphology is comparatively limited. This may have introduced eligibility misclassification and precludes direct comparison with MRI-based trials in this literature; future resource-limited-setting trials should incorporate MRI in at least a validation subset. As with comparable trials in this literature, the open-label nature of the interventions precludes participant and clinician blinding; outcome-assessor blinding was used to mitigate detection bias, but performance and placebo-response effects cannot be excluded. A further limitation is the small, single-centre sample (n = 14 per group), powered for the primary pain outcome only; secondary and exploratory findings should be regarded as hypothesis-generating. The 6-month follow-up does not inform longer-term durability or late recurrence.

Future multicentre trials with larger cohorts should explore the predictive value of patient-level variables —such as chronicity, baseline inflammation markers, and MRI-based structural changes—on treatment response. Comparative studies against corticosteroid, botulinum toxin, or arthroscopic interventions could further refine the therapeutic algorithm for TMJ-ID. In addition, mechanistic studies examining cytokine profiles and proteomic changes in synovial fluid before and after I-PRF + HA treatment could deepen our understanding of the biological pathways underlying clinical improvements.

In this small randomised trial, combining I-PRF with HA after TMJ arthrocentesis was associated with the most consistent improvements in pain, function and quality of life, and I-PRF alone also performed well. These findings are preliminary and warrant confirmation in larger, MRI-validated, multicentre trials.

Declarations

Ethics approval

This study was performed in accordance with the ethical standards laid down in the 1964 Declaration of Helsinki and its later amendments. Approval was granted by the Institutional Ethics Committee of Vishnu Dental College, Bhimavaram, India (No. IECVDC/23/PG01/OMFS/IVV/30).

Consent to participate

Written informed consent was obtained from all individual participants included in the study.

Consent to publish

The authors affirm that human research participants provided informed consent for publication of the images in Online Resource 1 (Figs. S1–S4).

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Competing Interests

The authors have no relevant financial or non-financial interests to disclose.

Data availability

The datasets generated and/or analysed during the current study are available from the corresponding author on reasonable request.

AI-use statement:

Large language model assistance (Claude, Anthropic) was used for language editing and grammatical corrections. The authors reviewed all content and take full responsibility for the final manuscript

Author contributions

Manoj K Malya and Divya Puvvada contributed to the study conception and design. Material preparation, data collection and clinical procedures were performed by Manoj K Malya, Divya Puvvada, Uddarraju Shivaji Raju, Kishore Moturi and Siva Dilip Sami. Statistical analysis was performed by Manoj K Malya, Divya Puvvada and Pampana Sravani. The first draft of the manuscript was written by Manoj K Malya and Pampana Sravani, and all authors commented on previous versions of the manuscript. All authors read and approved the final manuscript.

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Figures

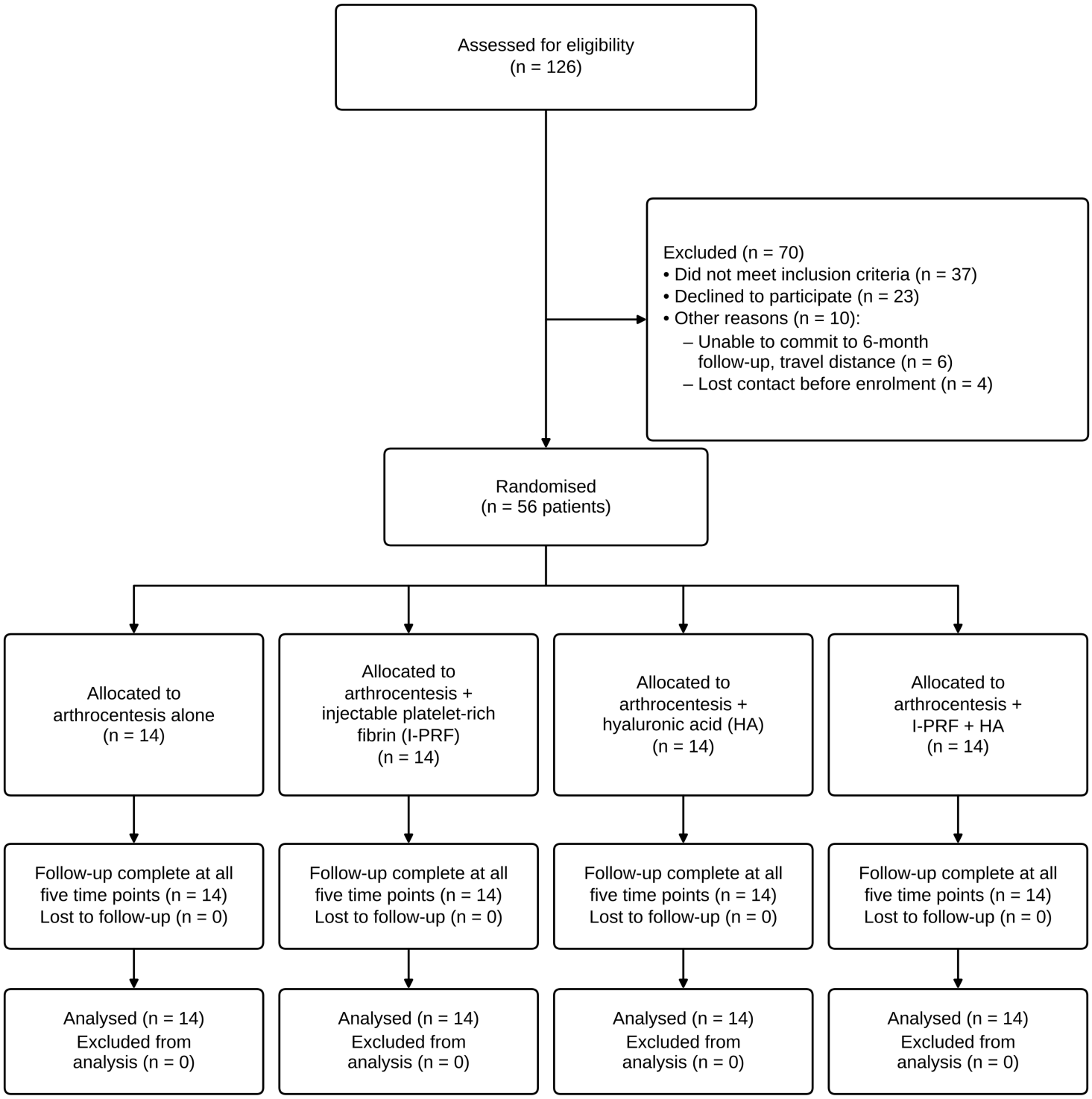


Figure 1

CONSORT flow diagram of participant screening, randomisation, allocation, follow-up and analysis. I-PRF, injectable platelet-rich fibrin; HA, hyaluronic acid

Supplementary Files

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