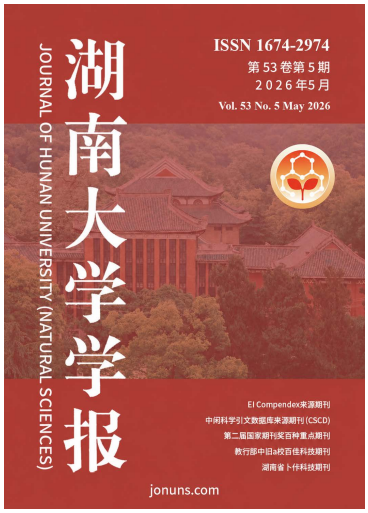

Journal of Hunan University

(Natural Sciences)

Vol. 53 No. 5

May 2026

Available online at

https://jonuns.com

Open Access Article

https://doi.org/10.55463/issn.1674-2974.53.5.9

Clinical Outcomes of Adjunctive Glucosamine-Chondroitin-MSM Supplementation Following Arthrocentesis and Intra-Articular Hyaluronic Acid Injection in TMJ Internal Derangement: A Randomized Clinical Trial

Abdelaziz Yahia Abou-Srea Mohamed [1], Hossam El-Dein Mohamed Ali [2*], Mohamed Alaa Eldin Mohamed [3*]

[1] Dentist, Ministry of Health, Egypt; Faculty of Dental Medicine, Al-Azhar University (Assiut Branch), Assiut, Egypt,
[2] Professor of Oral and Maxillofacial Surgery, Faculty of Dental Medicine, Al-Azhar University (Assiut Branch), Assiut, Egypt,
[3] Lecturer of Oral and Maxillofacial Surgery, Faculty of Dental Medicine, Al-Azhar University (Assiut Branch), Assiut, Egypt,

* Corresponding author: Zezoooyehia19@gmail.com

Article History:

Received: March 7, 2026
Revised: April 28, 2026
Accepted: May 14, 2026
Published: May 29, 2026

Abstract: Temporomandibular joint (TMJ) internal derangement is a common cause of pain and functional limitation that can negatively affect quality of life. Arthrocentesis combined with intra-articular hyaluronic acid (HA) injection is widely used as a minimally invasive treatment; however, the additional benefit of oral glucosamine–chondroitin–methylsulfonylmethane (GCM) supplementation remains uncertain. This randomized clinical trial included 30 patients with TMJ internal derangement who were randomly allocated to two equal groups. The intervention group received arthrocentesis followed by intra-articular HA injection combined with oral GCM supplementation for three months, whereas the control group received arthrocentesis with HA injection alone. Pain intensity was evaluated using the Visual Analog Scale (VAS), and maximum mouth opening (MMO) was measured at baseline and at 1 week, 1 month, 3 months, and 6 months after treatment. Both groups demonstrated statistically significant reductions in pain and improvements in MMO over time ($p < 0.001$). Although absolute pain and MMO

values differed between groups at certain follow-up intervals, comparisons of changes from baseline revealed no statistically significant differences between the two treatments ($p > 0.05$). Within the limitations of this study, arthrocentesis combined with intra-articular HA injection was effective in improving clinical outcomes in patients with TMJ internal derangement, whereas adjunctive oral GCM supplementation did not provide additional measurable benefit during the 6-month follow-up period.

Keywords: temporomandibular joint; TMJ internal derangement; arthrocentesis; hyaluronic acid; glucosamine; chondroitin; methylsulfonylmethane; maximum mouth opening; clinical trial.

辅助性葡萄糖胺-软骨素-MSM 补充在颞下颌关节内部紊乱患者关节穿刺冲洗术及关节内透明质酸注射后的临床疗效：一项随机临床试验

摘要：

颞下颌关节（temporomandibular joint, TMJ）内部紊乱是导致疼痛和功能受限的常见原因，并可能对生活质量产生不利影响。关节穿刺冲洗术联合关节内透明质酸（hyaluronic acid, HA）注射被广泛用作一种微创治疗方法；然而，口服葡萄糖胺–软骨素–甲基磺酰甲烷（glucosamine-chondroitin-methylsulfonylmethane, GCM）补充治疗的额外获益仍不明确。本随机临床试验纳入了 30 例颞下颌关节内部紊乱患者，并将其随机分为两个等量组。干预组接受关节穿刺冲洗术后关节内 HA 注射，并联合口服 GCM 补充治疗 3 个月；对照组仅接受关节穿刺冲洗术联合 HA 注射。采用视觉模拟评分法（Visual Analog Scale, VAS）评估疼痛强度，并在基线以及治疗后 1 周、1 个月、3 个月和 6 个月测量最大张口度（maximum mouth opening, MMO）。两组患者随时间推移均表现出疼痛显著减轻和 MMO 显著改善（$p < 0.001$）。尽管在某些随访时间点，两组之间的绝对疼痛评分和 MMO 数值存在差异，但与基线相比的变化量比较显示，两种治疗方案之间无统计学显著差异（$p > 0.05$）。在本研究的局限性范围内，关节穿刺冲洗术联合关节内 HA 注射可有效改善颞下颌关节内部紊乱患者的临床结局，而辅助性口服 GCM 补充治疗在 6 个月随访期间未显示出额外的可测量获益。

关键词：

颞下颌关节；颞下颌关节内部紊乱；关节穿刺冲洗术；透明质酸；葡萄糖胺；软骨素；甲基磺酰甲烷；最大张口度；临床试验。

1. Introduction

Temporomandibular disorders (TMDs) are among the most prevalent causes of non-dental orofacial pain, affecting approximately 21.5–51.8% of the population (1, 2). Clinically, TMDs main characteristics include pain, joint sounds, and limitation of mandibular movements, often negatively affecting sleep quality and increasing anxiety levels, thereby impairing overall quality of life (3, 4). Among TMD subtypes, internal derangement of the temporomandibular joint (TMJ), particularly anterior disc displacement with or without reduction, is commonly encountered (5). Disc displacement with reduction is typically associated with clicking during mandibular movement, whereas disc displacement without reduction frequently leads to painful joint locking and restricted mouth opening (6).

The underlying pathophysiology of TMJ internal derangement involves inflammatory and degenerative changes within the joint. Elevated levels of interleukin-1β (IL-1β), interleukin-6 (IL-6), tumor necrosis factor-α (TNF-α), and prostaglandin E2 (PGE2) have been detected in the synovial fluid of affected joints, contributing to pain, cartilage degradation, and functional impairment. These inflammatory mediators are closely related to joint tenderness and limitation in maximum mouth opening (MMO), which represent primary clinical concerns for patients seeking treatment (7, 8).

Arthrocentesis with intra-articular hyaluronic acid (HA) injection has been increasingly adopted as a minimally invasive treatment modality for TMJ internal derangement (9). Arthrocentesis facilitates lysis of

adhesions, removal of inflammatory mediators, restoration of synovial fluid circulation, and improvement in joint mobility (10). Hyaluronic acid, a natural component of synovial fluid and cartilage matrix, enhances joint lubrication, reduces friction, and exerts anti-inflammatory and analgesic effects (11). Clinical studies have demonstrated remarkable reductions in terms of pain and enhancements in mandibular function following arthrocentesis combined with HA injection (9).

In addition to intra-articular therapies, oral supplementation with glucosamine, chondroitin sulfate, and methylsulfonylmethane (GCM) has been investigated as a disease-modifying and symptomatic treatment approach for degenerative joint conditions (12). Glucosamine serves as a precursor for glycosaminoglycan synthesis and may inhibit inflammatory mediators such as PGE2 and IL-1β. Chondroitin sulfate contributes to cartilage matrix integrity and collagen synthesis while suppressing degradative enzymes (13). Methylsulfonylmethane (MSM) exhibits anti-inflammatory and antioxidative properties and has shown symptomatic improvement in osteoarthritic conditions (14). Previous reports indicate that glucosamine-chondroitin combinations may reduce TMJ pain, clicking, and crepitus, supporting their potential role in TMJ internal derangement management (9).

Despite the documented benefits of intra-articular HA injection and oral GCM supplementation when used individually, evidence regarding their combined use in TMJ internal derangement remains limited. More specifically, the remaining clinical question is whether oral glucosamine–chondroitin–methylsulfonylmethane supplementation provides an additional measurable benefit when added to an already established minimally invasive treatment protocol, namely arthrocentesis followed by intra-articular hyaluronic acid injection.

Therefore, the novelty and clinical contribution of the present randomized clinical study lie in evaluating whether adjunctive oral GCM supplementation can enhance pain reduction and functional recovery beyond the improvement achieved by arthrocentesis with intra-articular HA injection alone. Clarifying this issue is clinically relevant because demonstrating either an added benefit or a neutral effect may help guide evidence-based treatment planning, avoid unnecessary medication use, and support rational decision-making in patients with TMJ internal derangement. Accordingly, the primary outcome measures of this study were pain reduction using the visual analog scale (VAS) and improvement in maximum mouth opening (MMO).

2. Patients and Methodology

Study Design and Setting

This randomized controlled clinical study was conducted on 30 adult patients diagnosed with temporomandibular joint (TMJ) internal derangement, including disc displacement with or without reduction. Diagnosis was established based on clinical examination and magnetic resonance imaging (MRI). Patients presented with pain, joint sounds (clicking), limitation in maximum mouth opening (MMO), and mandibular deviation or deflection during opening.

The study was carried out at the Department of Oral and Maxillofacial Surgery, Faculty of Dental Medicine, Al-Azhar University (Assiut Branch).

Ethical Approval

The study protocol was reviewed and approved by the Institutional Ethical Committee of the Faculty of Dental Medicine, Al-Azhar University (Assiut Branch). All participants were informed about the study objectives, procedures, and potential risks. Written informed consent was obtained from all patients prior to inclusion in the study.

Eligibility Criteria

Eligibility criteria of the patients included age older than 18 years, diagnosed clinically and radiographically with TMJ internal derangement (unilateral or bilateral), and had previously undergone non-invasive conservative management without satisfactory improvement.

Patients were excluded if they had systemic diseases affecting joint healing, previous TMJ surgery or invasive TMD treatment, history of maxillofacial trauma, contraindications to MRI examination, hypersensitivity to study materials, or were completely or partially edentulous.

Randomization and Group Allocation

After confirmation of eligibility and obtaining written informed consent, the included participants were randomly allocated into two equal groups (n = 15 each) using a simple coin-toss method. Randomization was performed by an independent staff member who was not involved in outcome assessment or statistical analysis. A “heads” result assigned the patient to the study group, whereas a “tails” result assigned the patient to the control group.

Because of the nature of the intervention, complete patient blinding was not feasible, as patients in the study group received additional oral GCM supplementation. Allocation concealment was limited; however, group assignment was performed only after patient enrollment to reduce selection bias. Clinical outcome measurements, including pain score assessment and maximum mouth opening measurement, were recorded according to a standardized follow-up protocol. The outcome assessor was kept unaware of the

allocation whenever possible during follow-up visits to minimize assessment bias.

Both groups received the same core intervention, consisting of arthrocentesis followed by intra-articular hyaluronic acid injection, as well as the same postoperative instructions and follow-up schedule. This was done to minimize performance bias, with the only planned difference between groups being the administration of oral glucosamine–chondroitin sulfate–methylsulfonylmethane supplementation in the study group.

Study Group: Received intra-articular hyaluronic acid (HA) injection combined with oral glucosamine–chondroitin sulfate–methylsulfonylmethane (GCM) supplementation.

Control Group: Received intra-articular HA injection only.

Preoperative Assessment

Clinical Evaluation

A comprehensive history was obtained, including demographic data, medical and dental history, previous treatments, medication use, parafunctional habits, and chief complaint.

Clinical examination included assessment of facial symmetry, mandibular movement, TMJ palpation (static and dynamic), and auscultation for joint sounds.

Maximum mouth opening (MMO) was measured in millimeters using a flexible plastic ruler with the patient seated upright and head supported. Both assisted and unassisted openings were recorded.

A visual analog scale (VAS) was employed for evaluation of pain intensity represented by numerical values from 0 (no pain) to 10 (worst imaginable pain).

Radiographic Evaluation

All patients underwent MRI examination prior to intervention. MRI was used to evaluate disc position, disc morphology, disc–condyle relationship, joint effusion, and joint integrity.

The disc-condyle relationship was considered normal when the posterior band of the disc was located at the 12 o'clock position relative to the mandibular condyle in the closed-mouth position, with the intermediate zone positioned between the condyle and the posterior slope of the articular eminence. In the open-mouth position, the intermediate zone was expected to remain interposed between the condyle and articular eminence.

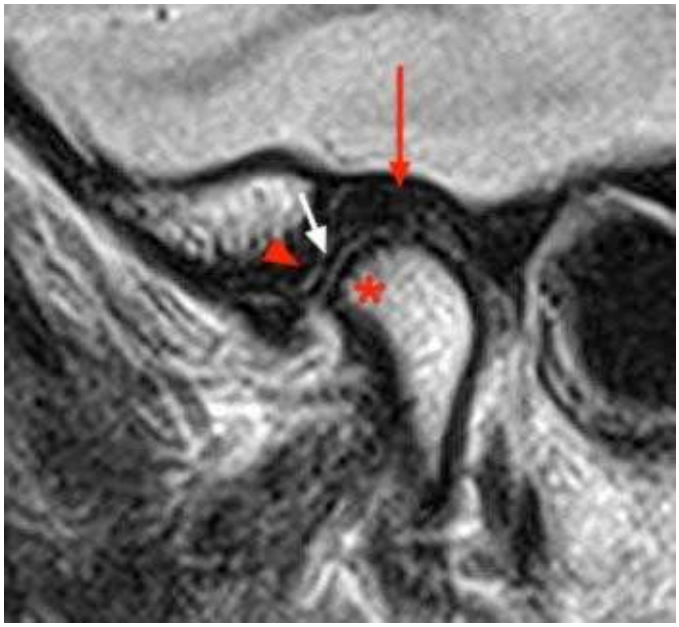

Figure 1: Magnetic resonance image demonstrating normal disc positioning within the temporomandibular joint. The posterior band of the articular disc (red arrow) is located superior to the mandibular condyle, while the intermediate zone (white arrow) is properly interposed between the condyle and the articular eminence. The anterior band is indicated by the red triangle. The red star denotes the normal articulation between the condyle and the articular eminence in the closed-mouth (rest) position.

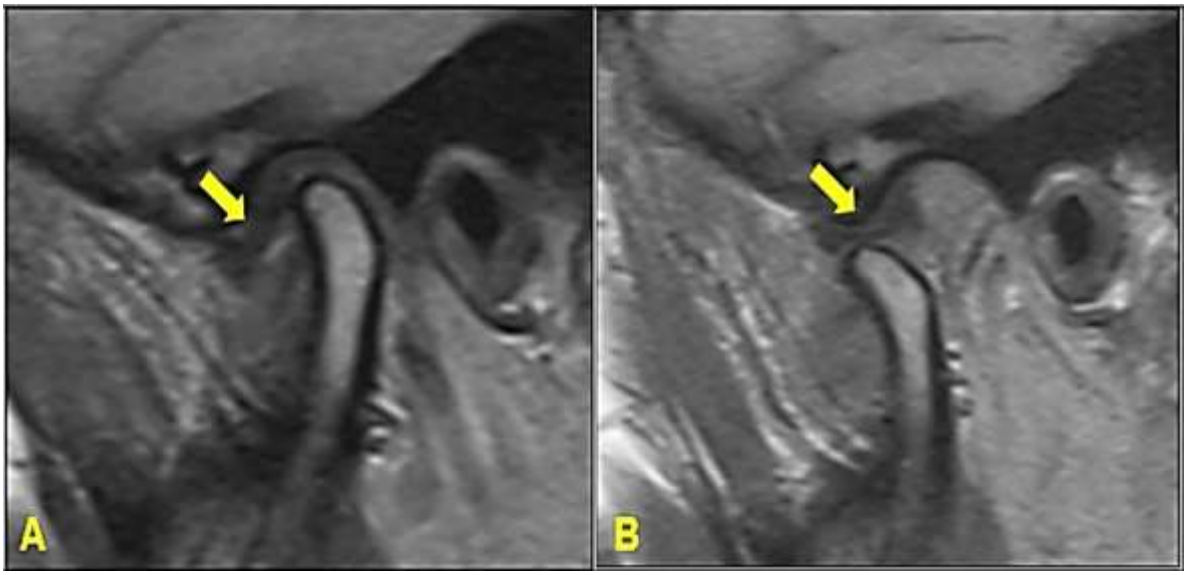

Figure 2: Magnetic resonance images illustrating anterior disc displacement with reduction (DDR).
(A) In the closed-mouth position, the articular disc is displaced anteriorly, with the intermediate zone positioned against the articular eminence only. (B) In the open-mouth position, the disc is recaptured and resumes its normal anatomical position between the mandibular condyle and the articular eminence. The yellow arrow indicates the articular disc.

Conservative Phase

Before surgical intervention, all participants underwent conservative management for a minimum duration of 1–2 months. Conservative therapy included patient education, dietary modifications, sleep improvement strategies, awareness of parafunctional habits, non-steroidal anti-inflammatory medications, muscle relaxants, physiotherapy, masticatory muscle massage, range-of-motion exercises, and occlusal stabilization splint therapy (2–4 mm thickness).

Intervention Procedures

Anesthesia

Povidone iodine was utilized for preauricular region disinfection. Auriculotemporal nerve block was administered using 3% mepivacaine without vasoconstrictor. Local anesthesia was delivered using a 27-gauge needle to ensure adequate analgesia before arthrocentesis.

Arthrocentesis Technique

Arthrocentesis was performed using the conventional double-puncture technique. Patients were positioned at a 45° angle with the head turned contralaterally. Two anatomical landmarks were identified along the cantho-tragal line.

An insertion of an 18-gauge needle into the superior joint space at the posterior point was carried out, followed by injection of Ringer's lactate to distend the joint cavity. Insertion of a second needle was carried out anteriorly to allow outflow. Lavage was performed using approximately 200 mL of Ringer's lactate solution to irrigate the superior joint compartment and remove inflammatory mediators and debris.

At the completion of lavage, 1.2 mL of hyaluronic acid (Hyalgan®, 20 mg/2 mL) was injected into the superior joint space. Mandibular manipulation in vertical, lateral, and protrusive directions was performed to promote adhesion release.

Pharmacologic Regimen

Patients in both groups received ibuprofen 600 mg postoperatively every 12 hours for the first 24 hours, then as needed.

In the study group, patients additionally received oral GCM supplementation for three months. Each tablet contained glucosamine 500 mg, chondroitin sulfate 400 mg, and methylsulfonylmethane 250 mg. Patients were instructed to take one tablet three times daily, corresponding to a total daily dose of glucosamine 1500 mg, chondroitin sulfate 1200 mg, and methylsulfonylmethane 750 mg. Supplementation was started after the arthrocentesis and intra-articular HA injection procedure and continued throughout the three-month postoperative period.

Patients were advised not to use any additional oral joint supplements, intra-articular injections, or unprescribed anti-inflammatory medications during the follow-up period. Compliance with GCM supplementation was monitored during follow-up visits by direct questioning and review of tablet intake. Any reported adverse effects, including gastrointestinal discomfort, allergic reactions, or intolerance to the supplement, were recorded throughout the study period.

Postoperative Care

All patients were instructed to apply intermittent ice packs during the first 24 hours, followed by warm packs for four days. A soft diet was advised, along with range-of-motion exercises during the first postoperative week. Occlusal stabilization splints were placed immediately after the procedure and maintained for one week.

Follow-Up Protocol

Clinical evaluation was performed preoperatively, immediately postoperatively, and at 1 week, 1 month, 3 months, and 6 months. Primary outcome measures were Pain score (VAS) and Maximum mouth opening (MMO). MRI was used as a diagnostic and supportive follow-up tool. Preoperative MRI was performed to confirm the diagnosis of TMJ internal derangement and to evaluate disc position, disc morphology, disc–condyle relationship, joint effusion, and joint integrity. Follow-up MRI was performed in selected cases at 3 and/or 6 months postoperatively to provide descriptive assessment of disc position, joint effusion, and inflammatory changes. However, MRI findings were not analyzed as a primary quantitative endpoint.

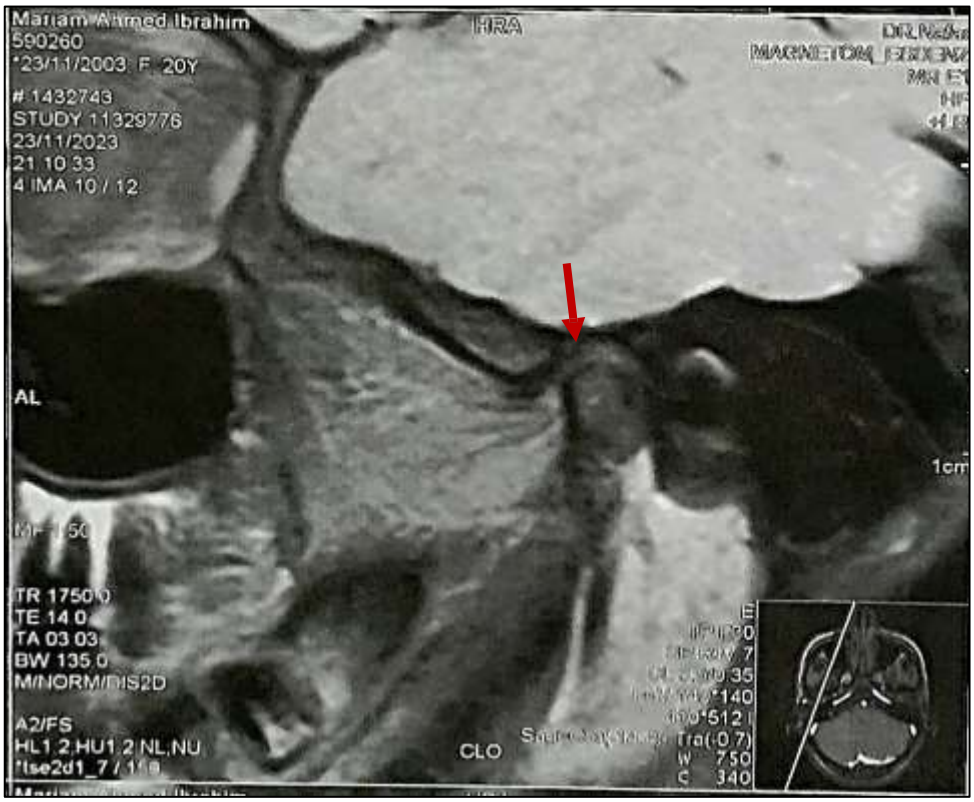

Figure 3: Sagittal T1-weighted MRI obtained at the 3-month follow-up for a patient in the study group, demonstrating the temporomandibular joint in the closed-mouth position. The red arrow indicates the position of the articular disc.

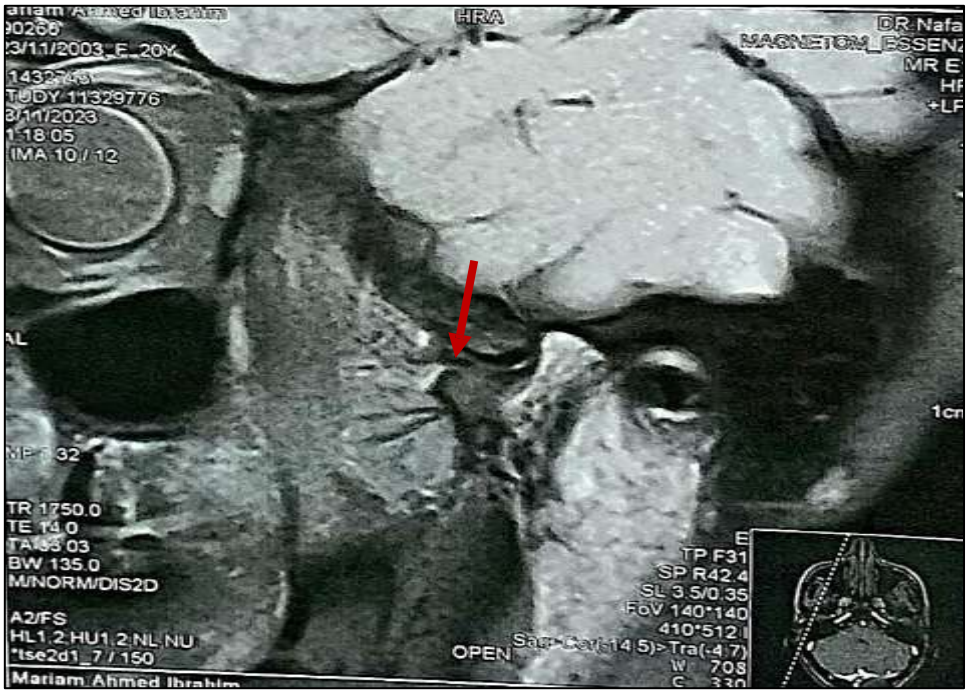

Figure 4: Sagittal T1-weighted MRI obtained at the 3-month follow-up for a patient in the Control group, demonstrating the temporomandibular joint in the closed-mouth position. The red arrow indicates the position of the articular disc.

Statistical Analysis

Statistical analysis was performed using SPSS version 26.0. Mean ± standard deviation or median was employed to express quantitative data along with interquartile range when appropriate. Categorical data were presented as frequencies and percentages. Comparisons between related groups were conducted using paired Student's t-test. Repeated measures ANOVA followed by Bonferroni post-hoc test was applied for multiple time-point comparisons. Between groups comparison by independent t test. A p-value < 0.05 was deemed statistically significant.

3. Result

A total of 30 patients were enrolled in the present randomized clinical trial and completed the follow-up period. The study population included 22 females (73.3%) and 8 males (26.7%), indicating a predominance of female patients. Participants were randomly allocated into two equal groups: the study group and the control group (n = 15 each).

The mean age of patients in the study group was 28.6 years, whilst the control group had a mean age of 30.2 years, reflecting comparable age distribution between both groups.

With respect to the type of temporomandibular joint internal derangement, 18 patients (60%) were diagnosed with disc displacement with reduction, whereas 12 patients (40%) presented with disc displacement with no reduction evident.

At baseline, no statistically significant difference in pain score was observed between the study and control groups (p = 0.099), confirming baseline comparability (Table 1).

Both groups demonstrated a statistically significant reduction in pain scores over time (p < 0.001 for both groups, repeated measures ANOVA) (Table 1). Within-group analysis revealed highly significant reductions from baseline at all postoperative intervals in both groups (p < 0.001).

Although absolute between-group comparisons showed significantly lower pain scores in the control group at 1 week, 1 month, 3 months, and 6 months, interpretation of treatment efficacy was based primarily on change from baseline, because baseline values were not completely identical between groups. When pain reduction from baseline was analyzed, no statistically significant difference was found between the study and control groups at any follow-up interval (p > 0.05), indicating that adjunctive GCM supplementation did not produce a statistically significant incremental pain-reduction effect beyond arthrocentesis with intra-articular HA injection alone (Table 2).

Baseline MMO values were comparable between both groups (p = 0.207), indicating no significant difference prior to intervention (Table 3).

Both groups exhibited statistically significant increases in MMO over time (p < 0.001 for both groups) (Table 3). Significant improvement compared to baseline was observed at all postoperative intervals in both groups (p < 0.001).

Similarly, although absolute MMO values were significantly higher in the study group at selected follow-up points, including 1 week, 3 months, and 6 months, these absolute comparisons should be interpreted cautiously because baseline MMO values were not identical between groups. When MMO gain from baseline was evaluated, no statistically significant difference was detected between the study and control groups at any time point (p > 0.05). Therefore, adjunctive GCM supplementation did not demonstrate a statistically significant incremental functional benefit beyond the improvement achieved by arthrocentesis with intra-articular HA injection alone (Table 4).

Table (1) Comparison between studied groups regarding pain score at different times

Time Point	Study Group (N=15)	Control Group (N=15)	t value	Between-Group p-value
Baseline	7.25 ± 0.71	6.38 ± 1.76	1.71	0.099
1 Week	4.75 ± 0.46#	4.00 ± 0.76#	3.14	0.004*
1 Month	3.62 ± 0.52#	2.12 ± 0.35#	8.96	<0.001*
3 Months	2.50 ± 0.53#	1.44 ± 0.18#	7.63	<0.001*
6 Months	2.12 ± 0.35#	1.38 ± 0.23#	6.72	<0.001*

P value over time	<0.001*	<0.001*		

_ Data expressed as Mean ± SD, _* significant at p value <0.05, _# significant difference with baseline values

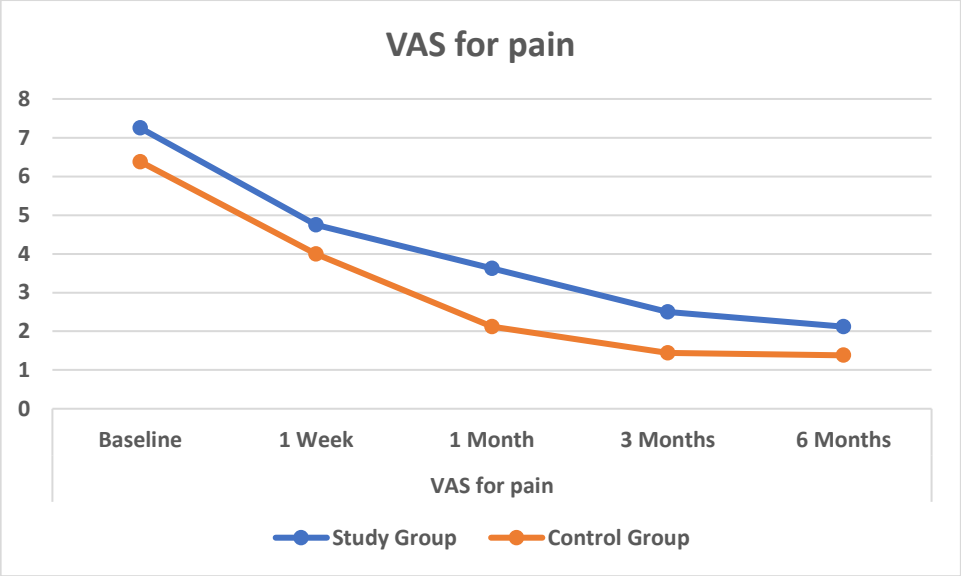

Fig (5) Line chart represents comparison of VAS score between studied groups

Table 2. Comparison of Pain Reduction from Baseline Between Study and Control Group

Time Point	Study (Mean Change ± SD)	Within-Group p-value (Study)	Control (Mean Change ± SD)	Within-Group p-value (Control)	Between-Group p-value
1 Week	-2.50 ± 0.76	< 0.001*	-2.37 ± 1.40	0.002*	0.828 (NS)
1 Month	-3.62 ± 0.74	< 0.001*	-4.25 ± 1.58	< 0.001*	0.329 (NS)
3 Months	-4.75 ± 0.71	< 0.001*	-4.93 ± 1.76	< 0.001*	0.784 (NS)
6 Months	-5.12 ± 0.64	< 0.001*	-5.00 ± 1.87	< 0.001*	0.861 (NS)

_ Data expressed as Mean ± SD, _* significant at p value <0.05

Table 3. Comparison Between Study and Control Groups Regarding Maximum Mouth Opening (MMO, mm) at Different Time Points

Time Point	Study Group (n = 15) Mean ± SD	Control Group (n = 15) Mean ± SD	t-value	p-value (Between Groups)
Baseline	29.75 ± 4.46	31.87 ± 4.18	1.29	0.207

1 Week	42.75 ± 2.01#	41.43 ± 1.08#	2.17	0.039*
1 Month	42.81 ± 2.03#	41.81 ± 0.80#	1.77	0.088
3 Months	43.00 ± 1.48#	41.87 ± 0.99#	2.37	0.024*
6 Months	43.25 ± 1.25#	41.93 ± 0.90#	3.21	0.004*
P value over time	<0.001*	<0.001*		

_ Data expressed as Mean ± SD, _* significant at p value <0.05, _# significant difference with baseline values

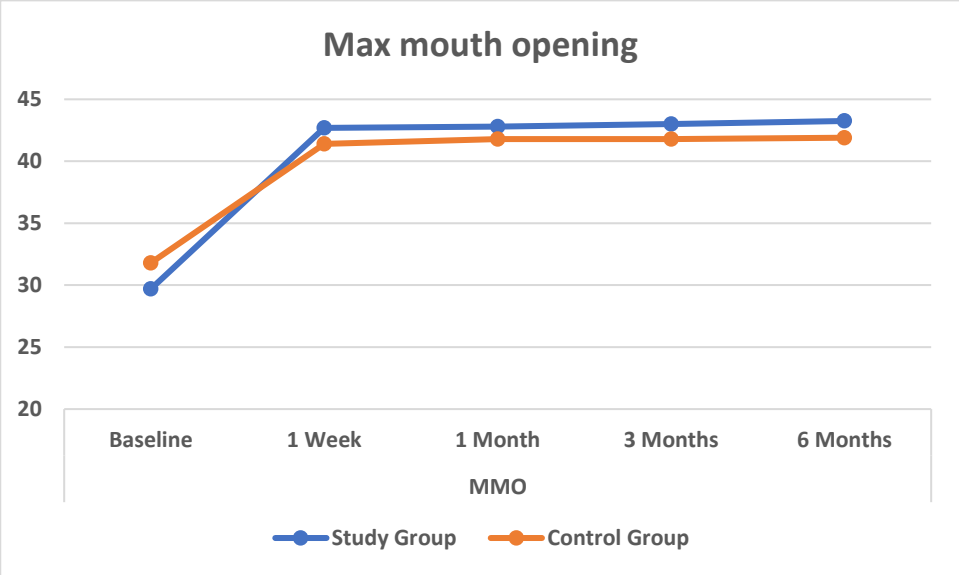

Fig (6) Line chart represents comparison of MMO between studied groups

Table 4. Comparison of MMO Gain (Change from Baseline) Between Study and Control Groups

Time Point	Study Group Mean Change ± SD (mm)	p-value (Within Study)	Control Group Mean Change ± SD (mm)	p-value (Within Control)	p-value (Between Groups)
1 Week	+13.00 ± 5.05	<0.001*	+9.56 ± 3.57	<0.001*	0.139 (NS)
1 Month	+13.06 ± 4.97	<0.001*	+9.93 ± 3.83	<0.001*	0.181 (NS)
3 Months	+13.25 ± 4.61	<0.001*	+10.00 ± 3.81	<0.001*	0.147 (NS)
6 Months	+13.50 ± 4.69	<0.001*	+10.06 ± 3.71	<0.001*	0.127 (NS)

_ Data expressed as Mean ± SD, _* significant at p value <0.05, NS: non-significant

4. Discussion

Temporomandibular joint (TMJ) internal derangement is a frequent cause of orofacial pain and functional limitation. Minimally invasive interventions particularly arthrocentesis with adjunct intra-articular agents, are widely utilized to reduce intra-articular inflammatory mediators, improve lubrication, and restore mandibular function. Contemporary clinical reviews continue to support arthrocentesis as an effective approach for improving pain and mouth opening, with pain reduction and increased maximal opening being among the most consistent outcomes (15, 16).

In the present randomized clinical study, both treatment protocols produced statistically significant clinical improvement over time. Pain scores showed a significant reduction in both groups across all follow-up intervals ($p < 0.001$), and MMO increased significantly in both groups ($p < 0.001$), reflecting a robust time-dependent therapeutic effect (Tables 1 and 3). These findings align with the established clinical rationale of arthrocentesis-based management, in which lavage and mobilization mechanisms may contribute to symptom relief and functional improvement (15, 16).

Although both groups improved, the between-group comparisons revealed important nuances. Absolute pain scores were significantly lower in the control group at 1 week, 1 month, 3 months, and 6 months (Table 1). Conversely, the study group showed significantly higher absolute MMO at selected follow-up points (Table 3). However, when treatment effect was evaluated using change-from-baseline ("gain"), neither pain reduction nor MMO improvement differed significantly between groups at any follow-up interval (Tables 2 and 4). This pattern suggests that both regimens were clinically effective, yet the adjunctive supplementation did not translate into a consistently greater incremental benefit when improvement was quantified relative to baseline.

A key explanation is that both groups received the same core intervention—arthrocentesis with intra-articular hyaluronic acid (HA) which has documented viscoelastic, anti-inflammatory, and lubrication-enhancing effects and can yield substantial improvements in pain and mandibular mobility (15, 16). In TMJ osteoarthritis (OA) populations, HA has also been reported to provide relatively rapid symptomatic relief compared with oral glucosamine-based regimens, further supporting its strong primary contribution to clinical improvement (17). Hence, the large improvement observed in both groups in this study may have reduced the ability to detect a modest additive effect from oral supplementation.

Regarding oral glucosamine and chondroitin, the literature remains mixed, and this inconsistency provides context for the neutral "gain" findings observed in our study. A large network meta-analysis in hip and knee OA concluded that glucosamine, chondroitin, and their combination did not show clinically meaningful analgesic benefit versus placebo or effect on structural outcomes (18). While OA data cannot be directly extrapolated to TMJ internal derangement, these results highlight ongoing uncertainty about the magnitude and consistency of benefit of these supplements across joint disorders.

In contrast, TMJ-specific clinical trials in degenerative TMJ conditions have reported potential benefit for glucosamine and/or chondroitin. For example, a randomized double-blind clinical trial investigated oral glucosamine hydrochloride and chondroitin sulfate for twelve weeks in TMJ conditions (including painful OA and disc-related diagnoses), suggesting a possible symptomatic role in certain patient subsets (19). More recently, a double-blind randomized controlled trial evaluated oral glucosamine hydrochloride combined with intra-articular hyaluronate sodium injection for TMJ OA, reflecting continued interest in a combined systemic + intra-articular strategy (20). Additionally, a systematic review focusing on oral glucosamine in TMJ OA summarized the literature as heterogeneous, emphasizing variability in protocols, endpoints, and certainty of evidence (21). Collectively, these studies suggest that any additional benefit of oral supplementation—if present—may depend on diagnosis (degenerative OA vs internal derangement), dosing, and duration, which could explain why an adjunct effect was not demonstrable in the current internal derangement cohort.

Another factor is treatment duration and follow-up timing. Oral glucosamine-based therapies may require longer administration or longer observation windows to manifest measurable differences, especially if the hypothesized mechanism relates to cartilage metabolism rather than rapid anti-inflammatory action. Notably, in TMJ OA, retrospective comparative work reported that HA injection achieved faster symptom relief and showed superior clinical effects compared with oral glucosamine plus diclofenac, while neither strategy clearly halted bony changes (17, 22). In our study, supplementation duration and follow-up intervals may therefore have been sufficient to capture the dominant early HA effect but insufficient to detect delayed systemic supplementation effects, particularly in a non-OA internal derangement population.

Safety outcomes in this trial were favorable, with no serious complications observed. This aligns with the broader clinical experience that arthrocentesis-based interventions are generally well tolerated when appropriately performed, although transient postoperative discomfort and localized reactions have been reported in other settings (15).

This study has limitations that should be considered when interpreting the findings. The sample

size may have limited statistical power to detect small between-group differences in "gain." Additionally, the follow-up duration, while clinically meaningful, may not fully reflect longer-term trajectories. Future trials with larger samples, longer supplementation durations, and stratification by internal derangement subtype (with vs without reduction) may clarify whether specific subgroups derive additional benefit from adjunctive oral supplements.

Within the limitations of this study, arthrocentesis followed by intra-articular HA injection produced remarkable favorable prognosis with respect to pain and MMO. However, the addition of oral glucosamine–chondroitin–methylsulfonylmethane supplementation did not confer a statistically significant advantage when outcomes were assessed as change from baseline. No formal sample size or power calculation was performed; therefore, the study may have been underpowered to detect small between-group differences in incremental treatment effects.

A further limitation is that radiographic follow-up was not available in a complete standardized dataset for all participants. Although MRI was used for diagnosis and supportive postoperative assessment, the study did not include formal quantitative analysis of disc position changes, joint effusion, inflammatory changes, or correlation between MRI findings and clinical outcomes. Accordingly, the radiographic images should be interpreted as illustrative supportive findings rather than as a structured radiographic outcome analysis. Future studies should include standardized MRI follow-up protocols and validated radiographic scoring systems.

5. Conclusion

Arthrocentesis followed by intra-articular hyaluronic acid (HA) injection significantly improved pain in addition to maximum mouth opening (MMO) in patients with temporomandibular joint (TMJ) internal derangement.

Although additional oral glucosamine–chondroitin–methylsulfonylmethane (GCM) supplementation resulted in clinical improvement, it did not provide statistically superior benefit compared with HA injection alone when assessed as change from baseline.

Therefore, arthrocentesis with HA injection remains an effective minimally invasive treatment for TMJ internal derangement, while adjunctive GCM supplementation did not demonstrate additional clinical advantage within the study follow-up period.

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Manuscript Information
Word count: 6,835 words (excluding references).
Peer-Review Record

Fast-track status: Not fast-tracked.
First-round reviews received: 3 reports.
Revision cycles completed: 3 rounds.
Final version submitted: May 14, 2026