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Randomised Controlled Trial

TMJ

Arthroscope-guided intra-articular injection of chitosan–hyaluronate gel mixture vs hyaluronic acid in the treatment of temporomandibular joint internal derangement: a randomized controlled clinical trial

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Abstract. This study compares the effectiveness of arthroscope-guided intra-articular injections of sodium hyaluronic acid (HA) and chitosan–hyaluronate (CH) hybrid gel for patients with anterior disc displacement without reduction (ADDw/oR) of the temporomandibular joint (TMJ). A randomized controlled trial was conducted on 20 patients with symptomatic ADDw/oR. The study protocol was registered in the ClinicalTrials.gov (NCT06426199). Patients were randomly assigned in a 1:1 ratio to receive HA or CH injections following arthroscopic lavage. Randomization was computer-generated, allocation was concealed in sealed opaque envelopes, and outcome assessors were blinded. Outcomes (pain by VAS, maximum mouth opening (MMO), and lateral excursions) were assessed at baseline, 3 months, and 6 months. Both groups showed significant improvements in pain and joint function, while the CH group demonstrated superior outcomes, with greater increases in MMO (42.3 vs 33.6 mm at 3 months; 44.9 vs 37.1 mm at 6 months) and significantly lower pain scores (median 2 vs 3.5 at 6 months; $P = 0.032$). Lateral excursions improved in both groups, with the CH group showing more consistent progress. Joint clicking showed no significant differences. The CH gel provided more significant and sustained improvements in MMO and pain relief compared to HA. Its regenerative properties, prolonged therapeutic effects, and ability to enhance joint lubrication suggest CH as a promising alternative for managing TMJ internal derangements.

Keywords: Temporomandibular joint disorders; Arthroscopy; Chitosan; Hyaluronic acid; Randomized controlled trial; Pain measurement; Range of motion; Articular; Drug delivery systems.

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Symptomatic disc displacement without reduction (ADDw/oR) is characterized by pain during forced mouth opening and loading of the affected joint, due to overloading and stretching of the highly innervated retrodiscal tissue[1]. This condition significantly impairs quality of life, manifesting as pain, restricted jaw mobility, and functional impairment. Conventional minimally invasive treatments, including arthrocentesis and arthroscopy, aim to relieve symptoms through joint lavage and mobilization. Almorraisi et al., in a systematic review, concluded that arthroscopic lysis and lavage have superior efficacy in improving maximum interincisal opening (MIO) and reducing pain compared to arthrocentesis, with comparable rates of postoperative complications[2].

Hyaluronic acid (HA), a natural component of synovial fluid, plays a central role in joint lubrication, anti-inflammation, and pain modulation[3]. Intra-articular HA injections (visco-supplementation) have been widely used in the management of temporomandibular joint (TMJ) disorders owing to their anti-inflammatory and lubricating properties[4]. However, their clinical effect is often short-lived, necessitating repeated injections, which increase patient burden, healthcare costs, and the risk of complications[5,6].

Recent advances in biomaterials, particularly chitosan, have introduced new opportunities for sustained-release intra-articular therapies. Chitosan, a natural biopolymer, is recognized for its biocompatibility, regenerative capacity, and ability to form hybrid hydrogels with HA. These hydrogels prolong HA release, enhance lubrication, and support cartilage repair, making them a promising alternative for TMJ management[7,8]. Despite growing interest in chitosan-based therapies, comparative clinical evidence with standard HA treatments in TMJ disorders remains limited.

The primary objective of this randomized controlled trial was to evaluate whether a chitosan–hyaluronate (CH) hybrid gel is superior to high-molecular-weight HA in improving maximum mouth opening (MMO) at 6 months in patients with ADDw/oR. Secondary outcomes included pain intensity measured by visual analogue scale (VAS) and lateral excursions at 3 and 6 months. We hypothesized that CH gel would be superior to HA in improving MMO and reducing pain over the 6-month follow-up.

Patients and methods

This study was a prospective, parallel-group, randomized controlled superiority trial with a 1:1 allocation ratio, conducted at the Faculty of Dentistry, Suez University, on a convenient sample of patients recruited from the outpatient clinics complex, Department of Oral and Maxillofacial Surgery, Faculty of Dentistry, Suez University, where they were evaluated and followed throughout the study. The study used the Consolidated Standards of Reporting Trials (CONSORT) 2025 guidelines.

Patients were recruited between January 2024 and March 2024, with the last follow-up completed in September 2024. Patients with symptomatic TMJ anterior disc displacement without reduction based on clinical symptoms and magnetic resonance imaging (MRI) evaluations refractory to conservative treatment were in the study group. The inclusion criteria were fully dentulous adults aged between 25 and 50 years, symptomatic anterior displacement without reduction, stage III–IV Wilkes classification (limited mouth opening < 35 mm, pain occurs on forced mouth opening, history of clicking, MRI examination reveals the disc in front of the condyle in both closed and open position). The exclusion criteria were patients with haematological or neurological diseases, inflammation or connective tissue diseases, head and neck malignancies, history of treatment of TMJ disease, or history of craniofacial surgery unrelated to internal derangement treatment.

The sample size was calculated based on the primary outcome: MMO at 6 months. Parameters were taken from prior literature used in our pre-study planning from Guarda-Nardini et al.[9] A mean difference of 6.5 mm was expected between groups, with a standard deviation of 4.9 mm. Using a two-sided test with $\alpha = 0.05$ and $\beta = 0.20$ (80% power), this corresponded to a standardized effect size (Cohen's *d*) of 1.33, yielding a required total sample of 20 patients (10 per group). Although secondary outcomes were also measured at 3 and 6 months, the sample size calculation was anchored to the 6-month MMO endpoint, representing the most clinically meaningful horizon. To evaluate the robustness of these assumptions, a sensitivity analysis was performed using smaller effect sizes (Cohen's $d = 1.0, 0.8, 0.6$). The corresponding required sample sizes are shown in (Table 1). This analysis highlights that while the study was adequately powered to detect a large effect, it would have been underpowered to detect moderate effects.

Randomization, allocation concealment, and blinding

Patients were randomly allocated in a 1:1 ratio to either the CH group or the HA group using a computer-generated sequence (rand.org). The sequence was prepared by an independent statistician not involved in recruitment or treatment, and allocation was concealed in sequentially numbered, opaque, sealed envelopes, opened only at the time of intervention. Patients received either HA or CH gel injected into the upper compartment of the TMJ cavity. While the operating surgeon was necessarily aware of group allocation, both patients and outcome assessors were blinded. Clinical measurements and data analysis were performed by investigators unaware of treatment assignment, minimizing detection bias. The flow of participants through the trial is shown in Fig. 1.

All patients underwent a detailed history of the TMJ and a comprehensive preoperative clinical evaluation. During the initial assessment, all participants were questioned regarding habitual chewing patterns; none reported consistent unilateral chewing. The patient's evaluation included four key assessments. First, patients self-evaluated their pain and jaw function using the VAS, ranging from 0 to 10, to compare preoperative and postoperative conditions. The scale

Table 1. Sensitivity analysis of the required sample size for different assumed effect sizes.

Assumed effect size (Cohen's *d*)	Required sample per group (80% power, $\alpha = 0.05$)	Interpretation
1.33	10	Achieved in this study (significant effect)
1.0	17	Adequate for a strong but smaller effect
0.8	25	Typical threshold for a significant effect
0.6	45	Moderate effect, underpowered with current sample size

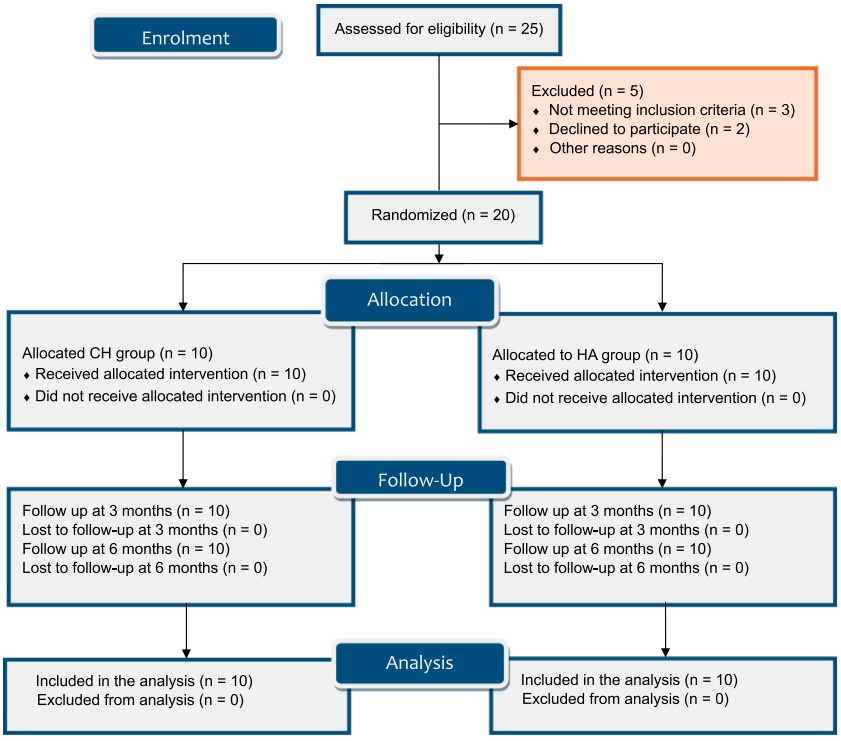

Fig. 1. CONSORT 2025 flow diagram of patient enrolment, randomization, follow-up, and analysis. CH, chitosan–hyaluronate; HA, hyaluronic acid.

categorized pain levels as follows: (0) no pain; (1–2) slight pain, where the patient is aware but not bothered; (3–4) mild pain, noticeable during activities; (5–6) severe pain, where the patient can still perform normal activities; (7–8) very severe pain, forcing the patient to stop regular activities; and (9–10) extremely severe pain, necessitating rest and halting all activities. Second, maximum lateral excursion was measured as the distance between the upper and lower midlines of the jaw, using a digital calliper, with the results averaged for both sides. Third, patients were asked to repeatedly open and close their mouths, noting whether clicking was present or absent. Fourth, a digital calliper measured MMO in millimetres between the upper and lower incisors. All patients underwent MRI preoperatively to evaluate the displacement. All patients were offered conservative treatment as the first line of treatment in all TMJ internal derangement cases, but only symptomatic cases refractory to conservative treatment were included.

Preparation of injectable materials

The lyophilized chitosan salt and CH hydrogel preparations were conducted by an experienced biochemist at the Natural and Medical Sciences Research Center, University of Nizwa, Oman. The lyophilized chitosan salt was prepared by solubilizing 1 g of pure chitosan in 1% acetic acid (1% w/w), stirring the mixture for 24 h at 25°C. NaOH 1 N was then added dropwise to the chitosan solution at 0°C to raise the pH of the solution to 6.2 without precipitating the chitosan. The solution was left overnight at 40°C and then lyophilized (by Alpha 1–2 LDplus) at 50°C for 24 h in a freeze-dryer[10].

The CH hydrogel preparation started with mixing and dissolving 76 mg of frozen dried chitosan biopolymer in 12 mL of phosphate-buffered saline (PBS) 10 mM (PH 7.0) using a magnetic stirrer for 90 min at 50 °C. Then the frozen-dried chitosan biopolymer was dissolved in PBS. The solution was left overnight at 4 °C. A total of 4 mL of this solution was mixed with 12 mL of Hyalogen gel (20 mg hyaluronic acid sodium salt) using a magnetic stirrer for 15 min; this hydrogel was then autoclaved for 15 min at 121 °C with a total cycle time of 35 min[11].

Arthroscopy procedure

Level I arthroscopy lysis and lavage surgical procedure was performed in Suez University Hospital. After the randomization procedures, the envelope was handed to the principal investigator and opened just before performing the surgical procedure. All interventions were performed by the same surgeon following a standardized operative protocol to minimize variability. The pre-auricular skin surface was disinfected with povidone–iodine solution, and arthroscopic arthrocentesis was performed under general anaesthesia via endotracheal intubation. For both groups, the procedure was carried out under general anaesthesia using a double-puncture technique. A line was drawn from the lateral canthus to the midtragus of the ear, referred to as the tragus-to-lateral-canthus line, to determine entry points at the 10–2 and 20–10 locations. The 10–2 point is located 10 mm from the tragus and 2 mm below the line, aligning with the posterior recess in the glenoid fossa. The 20–10 point is positioned 20 mm from the tragus and 10 mm below the line, corresponding to the prominence of the articular eminence. Initially, a diagnostic sweep was performed using a 1.9 mm, 30-degree arthroscope (Karl Storz Arthroscope, Karl Storz SE & Co. KG, Tuttlingen, Germany), which was inserted into a cannula with an inner diameter of 2.0 mm and an outer diameter of 2.2 mm.

The second puncture for the working cannula, also 2.0 mm in diameter, was created while the arthroscope illuminated the anterolateral aspect of the anterior recess. This puncture was precisely positioned at the most anterior and lateral corner of the superior joint space to ensure optimal flexibility for the operative cannula. The condyle remained seated in the fossa during the procedure. Afterward, the irrigation needle was removed, and the joint was insufflated with 2 mL of irrigation fluid to facilitate visualization.

The puncture site was determined using triangulation principles[12,13] with the orientation vectors forming an equilateral triangle to ensure accurate and safe placement of the second puncture. The depth of the arthroscope within the cannula was carefully measured not to exceed 25 mm, preventing inadvertent penetration through the medial surface of the TMJ capsule. A second measuring cannula was aligned flat against the skin, with its tip marked at 0 mm at the entry point and in a straight line with the arthroscope's plane. The depth of penetration was then transferred to the cannula, with 3–5 mm added based on the angle formed between the arthroscope and

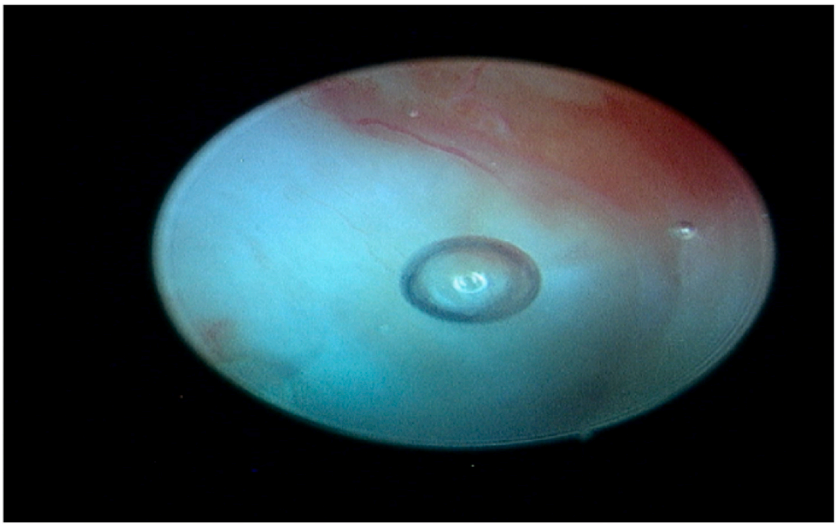

Fig. 2. An intra-articular clinical image captured through the arthroscope, illustrating the injection of chitosan–hyaluronate into the superior joint space.

the skin. The ideal position of the working cannula was parallel with the disc–synovial crease in the anterior recess to facilitate smooth operative procedures. Prior to the fossa puncture, the assistant insufflated the joint with an additional 2 mL of irrigation fluid. The trocar and cannula were inserted perpendicularly into the skin and advanced while maintaining the previously determined geometry and orientation. The trocar and cannula were inserted perpendicularly through the skin and advanced while maintaining the previously determined geometry and orientation. The trocar was then rotated through the soft tissue until it contacted bone at the junction of the anterior slope of the articular eminence and the continuation of the zygomatic arch. Unlike the fossa puncture, no excessive dissection of the periosteum was required at this site. Only the tip of the trocar contacted the cortical bone before being rotated through the capsule and synovium. Visualization of the trocar entering the joint space was confirmed on the monitor, after which the trocar was removed, and drainage of the irrigating fluid through the cannula was observed. The assistant stabilized the working cannula during the surgeon's instrumentation. Arthrocentesis was then performed using 100 mL of lactated Ringer's solution. Initially, 20 mL was introduced to stretch the capsule, followed by 80 mL for thorough lavage to eliminate inflammatory catabolites from the synovial fluid. For the first group, 2 mL of CH gel was injected into affected joints, and 2 mL of HA was injected into affected joints in the HA group (Fig. 2). Needles were removed after the injection, and the sites were covered with gauze dressing. Patients received non-steroidal anti-inflammatory drugs and muscle relaxants, used ice and warm packs on the jaw, performed gentle jaw exercises, followed a soft diet, and avoided hard or sticky foods. Follow-ups were done to assess TMJ clinically after 3 and 6 months. The primary outcome was MMO at 6 months. Secondary outcomes included pain intensity (VAS), lateral excursions, and joint clicking, assessed at baseline, 3 months, and 6 months.

Statistical analysis

Numerical data were examined for normality using both visual inspection of distribution plots and the Kolmogorov–Smirnov and Shapiro–Wilk tests. Variables following a normal distribution (MMO and lateral excursion) were summarized as mean ± standard deviation (SD), whereas non-normally distributed variables (pain scores) were expressed as median (range). Categorical data (joint clicking) were presented as frequencies and percentages. For normally distributed continuous variables, independent-sample *t*-tests were applied to compare outcomes between groups at each follow-up point. For non-normally distributed data, the Mann–Whitney *U*-test was used. Categorical outcomes were analysed using Fisher's exact test. Effect sizes for continuous outcomes were expressed as Cohen's *d*, calculated from pooled SDs and interpreted as small (≈0.2), moderate (≈0.5), or large (≥0.8). For categorical outcomes, the strength of association was expressed using Cramér's V. All analyses were two-sided, and statistical significance was set at $P \leq 0.05$. Statistical computations were performed using IBM SPSS Statistics for Windows, Version 23.0 (IBM Corp., Armonk, NY, USA).

Results

Twenty patients were enrolled and randomized equally between the two groups (HA = 10; CH + HA = 10). All participants completed the study and were analysed according to the group to which they were originally assigned (intention-to-treat analysis). Baseline demographic and clinical characteristics were comparable between the two groups (Table 2). The gender distribution was identical (seven females and three males in each group). The mean (SD) ages were 33.6 (7.1) years in the HA group and 36.3 (7.9) years in the CH + HA group.

Maximum mouth opening

At 3 months, the CH + HA group showed a significantly greater mean MMO than the HA group (mean difference = +8.7 mm; 95% CI +3.4 to +14.0; $P = 0.003$; Cohen's $d = 1.55$, large) (Table 3). At 6 months, this difference remained statistically and clinically significant (mean difference = +7.8 mm; 95% CI +4.5 to +11.1; $P < 0.001$; Cohen's $d = 2.24$, very large). These findings indicate superior mouth-opening improvement in the CH + HA group compared with the HA group (Fig. 3).

Pain scores

At 3 months, there was no statistically significant difference in VAS pain scores between the two groups ($P > 0.05$) (Table 4). At 6 months, patients in the CH + HA group reported significantly lower pain than those in the HA group (mean difference = –0.9 units; 95% CI –1.65 to –0.15; $P = 0.032$; Cohen's $d = 1.12$, large) (Fig. 4).

Joint clicking

Between-group comparisons showed no statistically significant difference in the frequency of joint clicking at any

Table 2. Descriptive statistics of participants' baseline characteristics.

Group	Patient no.	Age (years)	Sex	Mean age ± SD (range)	Female/male ratio
Hyaluronic acid (*n* = 10)	1	28	F	33.6 ± 7.1 (25–49)	7:3
	2	30	F		
	3	49	F		
	4	25	M		
	5	34	F		
	6	30	M		
	7	40	F		
	8	38	F		
	9	33	M		
	10	29	F		
Chitosan + hyaluronic acid (*n* = 10)	1	50	F	36.3 ± 7.9 (25–50)	7:3
	2	38	F		
	3	25	F		
	4	40	F		
	5	40	F		
	6	25	F		
	7	30	M		
	8	33	F		
	9	42	M		
	10	40	M		

SD, standard deviation.

follow-up (all $P > 0.05$) (Table 5). Cramér's V values were low (< 0.25), indicating a weak association between treatment group and clicking outcome.

Lateral excursion

At all time-points on both right and left sides, mean excursion values were similar in the two groups (all $P > 0.05$) (Table 6). Cohen's *d* values were small (≤0.4), suggesting no clinically relevant differences in lateral mandibular movement between groups.

Discussion

Findings of reduced HA molecular weight and concentration in arthritic joints led to injectable therapies, known as viscosupplementation, to restore the functional properties of synovial fluid. Moreover, mechanical stress or hypoxia can disrupt HA metabolism, reducing its molecular weight and impairing its lubricating function in TMJ disorders. For nearly two decades, intra-articular HA, also referred to as hyaluronan or sodium hyaluronate, has been employed as a treatment for TMJ disorders[14–16]. This study used Hyalgan, which contains high-molecular-weight hyaluronic acid (HMW HA), providing the necessary viscoelastic properties to improve the lubrication and reduce inflammation in the affected joint. HMW HA helps restore the normal properties of synovial fluid, supporting joint function and potentially relieving pain in osteoarthritis patients. However, HA's benefits are limited by its short duration of action. The most common viscosupplementation strategy is a series of either two intra-articular HA injections spaced 7–14 days apart[17–19], or five injections each 7 days apart[20,21]. The half-life of HA within the joint is very short, requiring repeated injections[6] which can lead to local toxicity, systemic side-effects, reduced quality of life, higher healthcare costs, and increased risk of complications. Slow-release intra-articular medications have the potential to eliminate many of these concerns. To address these issues, researchers are exploring prolonged drug-delivery systems to enable sustained release of HA, enhancing treatment effectiveness by reducing inflammation and promoting TMJ regeneration. Drug-delivery systems typically consist of an active therapeutic molecule, such as HA, and a carrier molecule. Three studies (one human and two animal studies) have explored chitosan's potential in treating TMJ disorders. In a human study, Li et al.[22] retrospectively compared 27 TMJ osteoarthritis patients receiving either chitosan or platelet-rich plasma (PRP) injections. Although both groups saw improved MIO and reduced pain over 6 months, PRP patients experienced greater MIO improvement and lower pain intensity. Both groups reported relief from TMJ sounds, but only the PRP group encountered transient complications, including TMJ pain, swelling, and occlusal changes. In an animal study by Li et al.[22], chitosan-based hydrogels showed significantly enhanced retention of hyaluronic acid compared to controls in rabbit TMJs, suggesting chitosan's efficacy as a controlled drug-release system. Another study by Li et al.[23] examined chitosan membranes' effects in goats following TMJ surgery, finding that these membranes prevented adhesions, preserved condylar integrity, and enabled greater mouth opening compared to controls with untreated adhesions. Chitosan's utility in tissue engineering for TMJ disorder treatment was evaluated in two additional studies. Bousnaki et al.[24] reported that chitosan/alginate promoted fibrocartilage tissue regeneration while Wu et al.[25] found that synovium-derived mesenchymal stem cells seeded in fibrin/chitosan scaffolds produced a fibrocartilaginous matrix, highlighting chitosan's regenerative potential for repairing TMJ disc perforations. Together, these studies highlighted chitosan's promise in

Table 3. Descriptive statistics and between-group comparison of maximum mouth opening (mm).

	HA (*n* = 10)		CH (*n* = 10)					
Time	Mean	SD	Mean	SD	Mean difference (CH − HA)	95% CI of difference	*P*-value	Cohen's *d* effect size
Preoperative	29.8	4.8	32.5	6.5	–	–	–	–
3 months	33.6	4.4	42.3	6.6	+8.7	+3.4 to +14.0	0.003[a]	1.55 (large)
6 months	37.1	3.9	44.9	3	+7.8	+4.5 to +11.1	< 0.001[a]	2.24 (very large)

HA, hyaluronic acid; CH, chitosan–hyaluronate hybrid gel; SD, standard deviation; CI, confidence interval.
[a]Significant at $P \leq 0.05$.

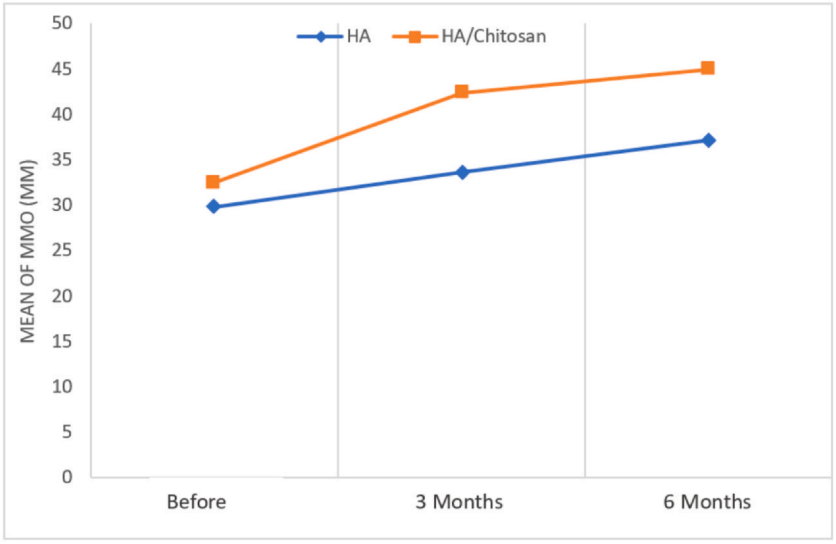

Fig. 3. Maximum mouth opening (MMO) measurements across different time-periods within each group.

TMJ disorder treatment, both as a therapeutic agent and as a scaffold for tissue engineering. In addition, chitosan exhibits antimicrobial properties by either penetrating bacterial cell walls and modulating gene expression or forming a nutrient-blocking polymeric membrane (HMW)[26]. It also accelerates wound healing by promoting clot formation, angiogenesis, and immune interactions while inhibiting matrix metalloproteinases to support tissue repair. Moreover, chitosan's structural similarity to articular cartilage components such as HA and glycosaminoglycans enables it to mimic the extracellular matrix and serve as a scaffold for cartilage repair[27,28]. This resemblance also makes chitosan valuable in bone tissue engineering, facilitating osteoconduction and promoting the deposition of mineral-rich matrices. A promising strategy involves chitosan-based hydrogel scaffolds, which integrate natural and synthetic materials to enable the sustained release of active molecules, potentially enhancing treatment effectiveness over the long term[29].

In the current study, both treatment modalities demonstrated significant improvements in pain reduction, MIO, and lateral excursion. However, the CH group consistently outperformed the HA group in key outcomes. The superior results in the CH group align with the regenerative and anti-inflammatory properties of chitosan. Chitosan's ability to inhibit matrix metalloproteinases and mimic the extracellular matrix structure likely contributed to prolonged therapeutic effects by promoting cartilage repair and joint stabilization. These findings are consistent with prior studies emphasizing the role of chitosan in reducing inflammation and enhancing joint lubrication[7,30]. The CH gel's sustained-release properties may have further augmented its efficacy, providing prolonged pain relief and improved jaw function compared to the transient effects typically observed with HA[11]. The significant increase in MIO over 6 months in the CH group highlights its potential for addressing restricted jaw mobility—a hallmark of ADDw/oR. While both groups exhibited time-dependent improvements, the CH group's performance was statistically superior, suggesting a more pronounced and durable impact on joint mechanics. This corroborates findings from Li et al.[31], who noted enhanced MIO and reduced adhesions with chitosan-based interventions in TMJ models. Pain reduction was another critical metric, with the CH group reporting significantly lower VAS scores at 6 months. This aligns with evidence supporting chitosan's role in modulating pro-inflammatory cytokines and reducing joint friction[32,33]. The prolonged analgesic effect of CH gel may stem from its dual-action mechanism: immediate joint lubrication and sustained anti-inflammatory activity. Lateral excursion improvements were comparable between groups, although the CH group showed more consistent progress over time. This underscores the hybrid gel's role in enhancing joint flexibility and mitigating structural limitations. Interestingly, joint clicking exhibited minimal variation across groups, with no significant differences at follow-up. This suggests that while both treatments alleviate pain and improve function, neither effectively addresses structural factors contributing to joint sounds. This finding aligns with earlier studies indicating that joint noise is often resistant to minimally invasive interventions[34].

The findings underscore the potential of CH gels as a viable alternative to HA in managing TMJ disorders. By offering enhanced regenerative properties, prolonged therapeutic effects, and greater patient satisfaction, CH gels may reduce the need for repeated interventions, addressing key limitations of traditional HA-based treatments.

Table 4. Descriptive statistics and between-group comparison of pain scores (visual analogue).

	HA (n = 10)		CH (n = 10)					
Time	Median (range)	Mean (SD)	Median (range)	Mean (SD)	Mean difference (CH − HA)	95% CI	P-value	Cohen's d effect size
Preoperative	7 (4–8)	6.4 (1.2)	7.5 (4–9)	7.4 (1.4)	–	–	–	–
3 months	4.5 (3–6)	4.6 (1)	4.5 (2–5)	3.9 (1.4)	–0.7	–2.3 to +0.9	0.361	0.40 (small)
6 months	3.5 (2–5)	3.5 (0.8)	2 (2–4)	2.6 (0.8)	–0.9	–1.65 to –0.15	0.032[a]	1.12 (large)

HA, hyaluronic acid; CH, chitosan–hyaluronate hybrid gel; SD, standard deviation; CI, confidence interval.
[a]Significant at $P \leq 0.05$.

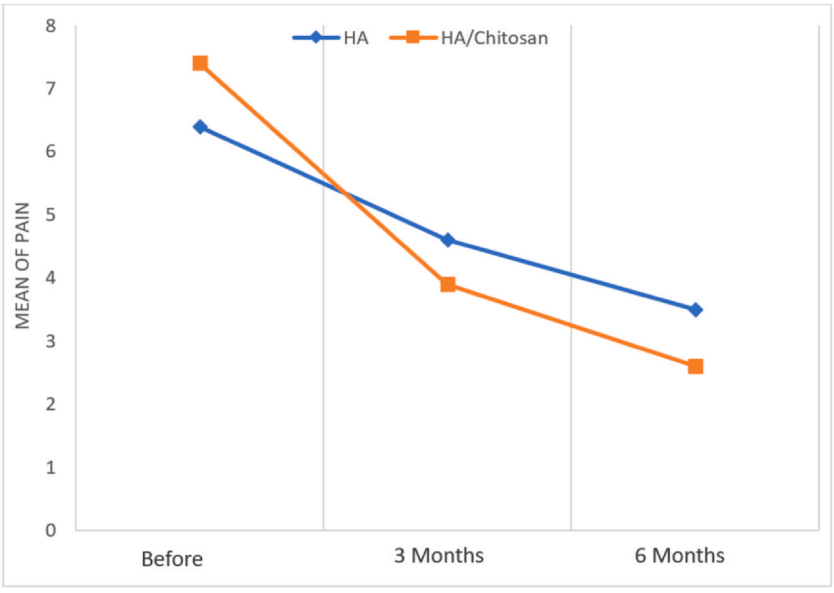

Fig. 4. Comparison of pain levels across various time-periods within each group.

However, this trial has certain limitations that warrant consideration. The sample size was calculated to detect a large effect size (d = 1.33) on the primary outcome, MMO at 6 months. While this was sufficient for the observed differences, detecting more moderate effects (d = 0.6–0.8) would have required larger groups. The results are therefore best interpreted as preliminary evidence that should be confirmed in larger multicentre studies. In addition, although outcome assessors were blinded, which helped reduce the detection bias risk, the operating surgeon was necessarily aware of group allocation, which may have introduced some risk of performance bias. Finally, the CH gel was prepared in-house at a university-affiliated laboratory. While this ensured consistency and sterility under controlled conditions, the absence of third-party quality control highlights the need for future studies using standardized commercial preparations to enhance reproducibility. Also, the follow-up period in this study was 6 months, which was sufficient to capture meaningful outcomes. Nonetheless, longer follow-up will be important in future trials to determine the durability of these improvements and the recurrence of symptoms. In conclusion, this randomized controlled trial provides preliminary evidence that CH gel may offer greater improvements in MMO and pain reduction than HA in the management of ADDw/oR. While these results are encouraging, they should be interpreted within the context of the trial's limitations, and further multicentre studies with longer

Table 5. Descriptive statistics and between-group comparison of joint clicking.

		HA (n = 10)		CH (n = 10)			
Time-point	Category	No.	%	No.	%	P-value	Cramér's effect size (V)
Preoperative	No clicking	5	50	6	60	–	–
	Crepitation	3	30	2	20		
	Painful clicking	2	20	2	20		
3 months	No clicking	6	60	8	80	0.628	0.218
	Painless clicking	4	40	2	20		
6 months	No clicking	6	60	8	80	0.628	0.218
	Painless clicking	4	40	2	20		

HA, hyaluronic acid; CH, chitosan–hyaluronate hybrid gel.

Table 6. Descriptive statistics and between-group comparison of lateral excursion (mm).

		HA (n = 10)		CH (n = 10)					
Side	Time	Mean	SD	Mean	SD	Mean difference (CH − HA)	95% CI	P-value	Cohen's d effect size
Right	Preoperative	9.3	1.77	9.4	2.32	–	–	–	–
	3 months	9.5	1.65	9.85	1.92	+0.35	–1.3 to +2.0	0.667	0.20 (small)
	6 months	9.5	1.65	9.85	1.92	+0.35	–1.3 to +2.0	0.667	0.20 (small)
Left	Preoperative	7.8	1.14	8.4	0.84	–	–	–	–
	3 months	8.7	1.49	9.1	0.99	+0.4	–0.8 to +1.6	0.490	0.31 (small)
	6 months	9.1	1.66	9.1	0.99	0.0	–1.3 to +1.3	1	0
Mean of the two sides	Preoperative	8.55	1.17	8.9	1.1	–	–	–	–
	3 months	9.1	1.22	9.48	0.61	+0.38	–0.6 to +1.4	0.396	0.40 (small)
	6 months	9.3	1.21	9.48	0.61	+0.18	–0.8 to +1.1	0.687	0.17 (small)

HA, hyaluronic acid; CH, chitosan–hyaluronate hybrid gel; SD, standard deviation; CI, confidence interval.

follow-up are needed to confirm and expand upon these findings.

Ethical approval

Obtained from the Suez Med Institutional Review Board (IRB) with ethical approval number 24.

Trial registration

The study protocol was registered in the Clinical Trials. Gov registry under No. NCT06426199.

Patient consent

Obtained.

Funding

None.

Data availability statement

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

Competing interests

None.

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