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Original Article

Clinical efficacy of intra-articular sodium hyaluronate injection and optimizing the puncture site in knee osteoarthritis

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Abstract: Objective: To evaluate the clinical efficacy of intra-articular sodium hyaluronate in knee osteoarthritis (KOA) and to assess the effect of different puncture sites on treatment outcome. Methods: This retrospective study included 198 patients with KOA treated between September 2023 and September 2025. Patients were divided into a sodium hyaluronate group (n=102) and a triamcinolone acetonide group (n=96). The sodium hyaluronate group was further categorized by puncture site: superolateral (n=26), inferolateral (n=25), superomedial (n=27), and inferomedial (n=24). Clinical outcomes were assessed at baseline and 6 months using the Western Ontario and McMaster Universities Osteoarthritis Index (WOMAC), Hospital for Special Surgery knee score (HSS), Arthritis Impact Measurement Scales 2-Short Form (AIMS2-SF), and inflammatory markers including interleukin-1 beta (IL-1β), C-reactive protein (CRP), and tumor necrosis factor alpha (TNF-α). Adverse events were recorded. Results: Baseline characteristics were comparable between groups (P>0.05). After 6 months, both treatments significantly improved clinical scores (P<0.05). The sodium hyaluronate group demonstrated superior pain relief, functional improvement, and lower incidence of adverse events compared with triamcinolone acetonide (P<0.05). In puncture-site analysis, WOMAC scores improved across all subgroups. The inferomedial approach provided greater pain relief, whereas the superolateral and superomedial approaches showed better improvement in joint stiffness, physical function, inflammatory markers, and quality of life (P<0.05). Adverse event rates did not differ among puncture-site groups. Conclusion: Intra-articular sodium hyaluronate is effective and safe for KOA. Clinical outcomes vary according to puncture site, with superolateral and superomedial approaches demonstrating consistent overall benefits.

Keywords: Knee osteoarthritis, sodium hyaluronate, triamcinolone acetonide, puncture site, clinical efficacy

Introduction

Knee osteoarthritis (KOA) is a common degenerative joint disease in older adults. Progressive cartilage degeneration, synovial inflammation, and structural joint damage lead to pain, stiffness, and functional impairment, significantly reducing quality of life [1, 2]. Intra-articular injection therapy is widely used in clinical practice to relieve symptoms while minimizing systemic adverse effects [3]. Triamcinolone acetonide and sodium hyaluronate are among the most commonly administered intra-articular agents [4]. Triamcinolone acetonide, a corticosteroid, has strong anti-inflammatory effects with analgesic properties. However, repeated or prolonged use may increase the risk of adverse events [5]. Sodium hyaluronate, a key component of synovial fluid, enhances joint lubrication, protects cartilage, suppresses the production of inflammatory substances, and is regarded generally as safe [6]. Evidence from randomized controlled trials and meta-analyses suggests that intra-articular sodium hyaluronate is associated with improvements in pain and joint function in patients with KOA, with benefits typically lasting 3-6 months and up to 6 months in some studies. In contrast, corticosteroids tend to provide greater short-term symptom relief, whereas sodium hyaluronate may offer relatively sustained functional improvement over time, particularly in mild-to-moderate KOA [7-9].

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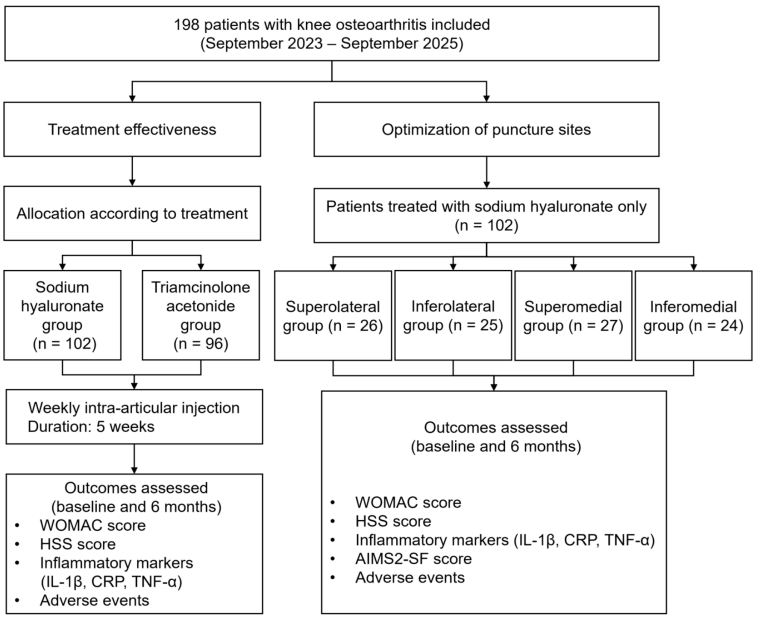

Figure 1. Flow chart of the study. Note: WOMAC: Western Ontario and McMaster Universities Osteoarthritis Index; HSS: Hospital for Special Surgery knee score; IL-1β: interleukin-1 beta; CRP: C-reactive protein; TNF-α: tumor necrosis factor alpha; AIMS2-SF: Arthritis Impact Measurement Scales 2-Short Form.

The clinical effectiveness of sodium hyaluronate used in the treatment of KOA might be affected by different interacting factors. Most previous studies have focused on comparisons between drug types and treatment regimens, while limited attention has been given to injection techniques, particularly puncture site selection. Given the high molecular weight and viscoelastic properties of sodium hyaluronate [10], differences in intra-articular distribution and retention at various puncture sites may affect clinical outcome. However, evidence regarding the optimal puncture site for sodium hyaluronate injection remains limited.

Therefore, this retrospective study aimed to evaluate and compare the clinical efficacy and safety of intra-articular sodium hyaluronate and triamcinolone acetonide in patients with KOA. In addition, different puncture sites in the sodium hyaluronate group were analyzed to explore their effect on clinical outcome, with the goal of optimizing intra-articular injection strategies in KOA.

Materials and methods

Study population

This retrospective study included 198 patients with knee osteoarthritis (KOA) who were treated at West Lake University Affiliated Hangzhou First People's Hospital Chengbei Campus between September 2023 and September 2025. The West Lake University Affiliated Hangzhou First People's Hospital Chengbei Campus Institutional Ethics Committee accepted the study protocol. The study flow chart is shown in **Figure 1**.

Inclusion criteria: (1) diagnosis of KOA according to the American College of Rheumatology criteria; (2) early- to middle-stage disease; (3) unilateral knee involvement; (4) age ≥18 years; (5) complete clinical data.

Exclusion criteria: (1) presence of obvious joint effusion, knee instability, or significant lower limb malalignment; (2) presence of systemic diseases, including diabetes mellitus, rheumatoid arthritis, severe cardiovascular disease, infection, or immune deficiency; (3) history of any lower limb surgery; (4) systemic or intra-articular corticosteroid medication within the last 3 months, or intra-articular sodium hyaluronate injection within the last 6 months.

Grouping

Patients were grouped according to the intra-articular medication they received in routine clinical practice. The 198 patients were categorized into a sodium hyaluronate group (n=102) and a triamcinolone acetonide group (n=96). Treatment decisions were made by the attending physicians based on clinical assessment. The two groups were compared to evaluate differences in clinical efficacy and safety.

Within the sodium hyaluronate group, patients were further classified according to the puncture site used during injection, including superolateral (n=26), inferolateral (n=25), superomedial (n=27), and inferomedial (n=24). The choice of puncture site was based on the physician's routine clinical practice. This subgroup analysis was performed to explore the effect of puncture site selection on outcome.

Table 1. Baseline demographic and clinical characteristics of the two groups

Variable	Sodium hyaluronate group (n=102)	Triamcinolone acetonide group (n=96)	$t/\chi^2/Z$	P
Age (years)	58.41±10.84	57.20±10.95	0.784	0.434
Sex, n (%)			0.109	0.742
Male	65 (63.73)	59 (61.46)		
Female	37 (36.27)	37 (38.54)		
Body mass index (kg/m^2)	22.99±3.15	23.24±3.06	-0.556	0.579
Disease duration (months)	20 (15, 24)	20 (15, 23)	-0.614	0.539
Kellgren-Lawrence grade, n (%)			0.092	0.955
I	38 (37.25)	37 (38.54)		
II	35 (34.34)	31 (32.29)		
III	29 (28.43)	28 (29.17)		

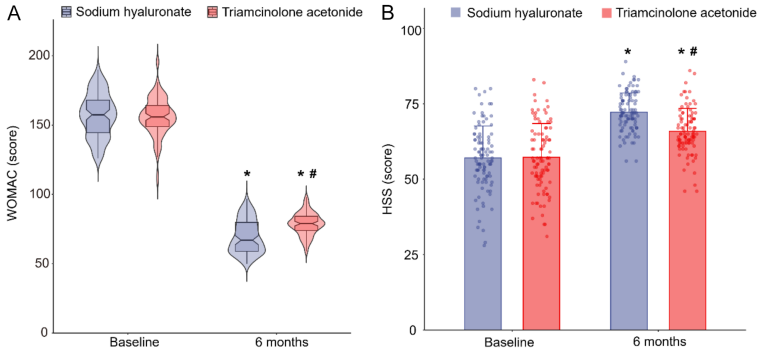

Figure 2. WOMAC and HSS scores in the sodium hyaluronate and triamcinolone acetonide groups. Note: *P<0.05 compared to the baseline value within the same group; #P<0.05 compared to the sodium hyaluronate group at the same time point; A: WOMAC; B: HSS.

Treatment procedures

Triamcinolone acetonide group: Patients received intra-articular injections of triamcinolone acetonide (2.5 mg; Kunming Jida Pharmaceutical Co., Ltd., China; approval No. H530-21604) once weekly for 5 weeks. After routine skin disinfection, the medication was slowly injected into the knee joint cavity using a standard intra-articular approach.

Sodium hyaluronate group: Patients received intra-articular injections of sodium hyaluronate (2.5 mL; Bloomage Freda Biopharm Co., Ltd., China; approval No. H20143093) once weekly for 5 weeks. After routine disinfection, injections were performed through different puncture sites. Patients were sat with their knees flexed for inferolateral and inferomedial approaches. The needle was placed close to the joint line lateral to the patellar tendon and pointed in the direction of the intercondylar notch. Patients were placed in the supine position with their knees extended for superolateral and superomedial approaches. The needle was inserted at an angle of roughly 45° toward the joint cavity, about 1 cm above and lateral to the superior patellar border.

Outcome measures

Primary outcome: Western Ontario and McMaster Universities Osteoarthritis Index (WOMAC): The WOMAC score was assessed at baseline and 6 months after treatment. The WOMAC consists of 24 items divided into three subscales: pain (5 items), stiffness (2 items), and physical function (17 items). Each item was scored on a 0-10 numeric rating scale, with higher scores indicating greater symptom severity. The total WOMAC score was calculated by summing all item scores, with higher total scores reflecting worse clinical status.

Secondary outcomes: Hospital for Special Surgery knee score (HSS): The HSS score was evaluated at baseline and 6 months after treatment to assess knee function. The HSS score ranges from 0 to 100 points and includes assessments of pain, function, range of motion, muscle strength, deformity, and stability. Higher scores indicate better knee function.

Inflammatory markers: Serum levels of interleukin-1 beta (IL-1β), C-reactive protein (CRP), and tumor necrosis factor alpha (TNF-α) were mea-

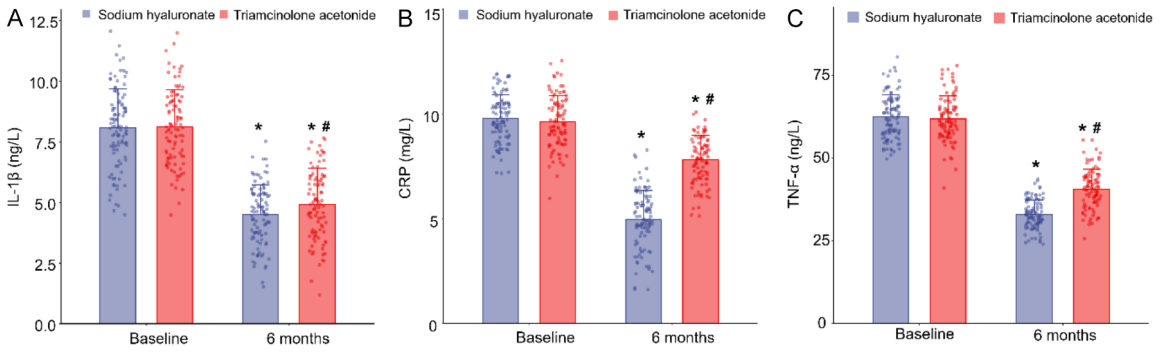

Figure 3. Inflammatory markers in the sodium hyaluronate and triamcinolone acetonide groups. Note: *P<0.05 compared to the baseline value within the same group; #P<0.05 compared to the sodium hyaluronate group at the same time point; A: IL-1β; B: CRP; C: TNF-α.

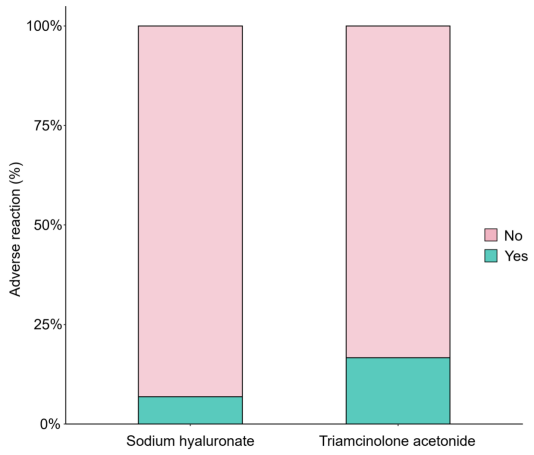

Figure 4. Adverse events in the sodium hyaluronate and triamcinolone acetonide groups.

sured at baseline and 6 months after treatment.

Arthritis Impact Measurement Scales 2-Short Form (AIMS2-SF): The AIMS2-SF questionnaire was used only for comparisons among different puncture-site subgroups in patients treated with sodium hyaluronate. It includes 26 items across five domains, with higher standardized scores indicating better quality of life.

Adverse events: Adverse events during treatment were recorded, including injection-site pain or swelling, bony tenderness, intra-articular hematoma, and joint movement limitation.

For comparisons between the sodium hyaluronate group and the triamcinolone acetonide group, outcome measures included WOMAC score, HSS score, inflammatory markers, and adverse events. In the subgroup analysis within the sodium hyaluronate group, outcome measures included WOMAC score, HSS score, inflammatory markers, AIMS2-SF score, and adverse events.

Statistical analysis

Statistical analyses were performed using SPSS version 26.0. Continuous variables were tested for normality. Normally distributed data are presented as mean ± standard deviation and were analyzed using the t test or analysis of variance. Non-normally distributed data are presented as median (interquartile range) and were analyzed using the nonparametric test. Categorical variables are expressed as number (percentage) and were compared using the chi-square test. P<0.05 was considered significant.

Results

Comparison of clinical efficacy between sodium hyaluronate and triamcinolone acetonide

Baseline characteristics: Among the 198 patients, 102 received sodium hyaluronate and 96 received triamcinolone acetonide. There were no significant variations between the two groups' baseline characteristics (all P>0.05; **Table 1**).

WOMAC and HSS scores: At baseline, no significant differences were observed between the two groups in terms of WOMAC or HSS score (P>0.05). Following 6 months of treatment, both groups demonstrated marked improvements in WOMAC and HSS scores; the

Table 2. Baseline characteristics of patients in different puncture-site groups

Variable	Superolateral group (n=26)	Inferolateral group (n=25)	Superomedial group (n=27)	Inferomedial group (n=24)	F/χ^2	P
Age (years)	59.35±9.65	56.24±10.73	59.07±11.67	58.41±10.84	0.442	0.723
Sex, n (%)					2.478	0.479
Male	16 (61.54)	19 (76.00)	15 (55.56)	15 (62.50)		
Female	10 (38.46)	6 (24.00)	12 (44.44)	9 (37.50)		
Body mass index (kg/m^2)	22.36±3.27	23.05±2.91	23.57±2.98	22.99±3.52	0.642	0.590
Disease duration (months)	18.88±6.65	20.92±6.34	18.11±7.41	19.46±7.85	0.724	0.540
Kellgren-Lawrence grade, n (%)					0.740	0.994
I	10 (38.46)	8 (32.00)	11 (40.74)	9 (37.50)		
II	9 (34.62)	10 (40.00)	8 (29.63)	8 (33.33)		
III	7 (26.92)	7 (28.00)	8 (29.63)	7 (29.17)		

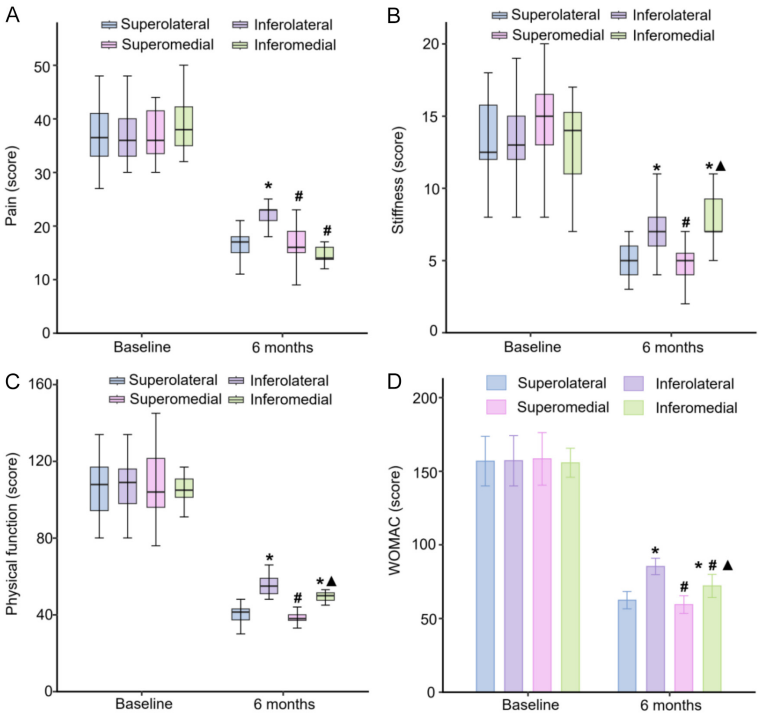

Figure 5. WOMAC scores in different puncture-site groups. Note: *P<0.05 compared to the superolateral group; #P<0.05 compared to the inferolateral group; ▲P<0.05 compared to the superomedial group; A: WOMAC pain score; B: WOMAC stiffness score; C: WOMAC physical function score; D: WOMAC total score.

magnitude of improvement was greater in the sodium hyaluronate group than in the triamcinolone acetonide group (P<0.05; **Figure 2**).

Inflammatory markers: At baseline, serum levels of inflammatory markers did not differ significantly between the two groups (P>0.05). After 6 months of treatment, levels of IL-1β, CRP, and TNF-α were significantly reduced in both groups, and were lower in the sodium hyaluronate group than in the triamcinolone acetonide group (P<0.05; **Figure 3**).

Adverse events: A total of 7 patients (6.68%) in the sodium hyaluronate group experienced adverse events, compared with 16 patients (16.67%) in the triamcinolone acetonide group during treatment. The sodium hyaluronate group demonstrated a significantly reduced rate of adverse events (χ^2=4.630, P=0.031; **Figure 4**).

Optimal puncture site for sodium hyaluronate injection

Baseline characteristics of puncture-site subgroups: Among the 102 patients treated with sodium hyaluronate, 26 were in the superolateral group, 25 in the inferolateral group, 27 in the superomedial group, and 24 in the inferomedial group. There were no significant variations among the four groups' baseline characteristics (all P> 0.05; **Table 2**).

WOMAC scores among puncture-site subgroups: After treatment, WOMAC pain, stiffness, physical function, and total scores improved significantly in all groups (P<0.05). The inferolateral group had higher pain scores than the other groups. Stiffness, physical function, and total WOMAC scores were higher in the

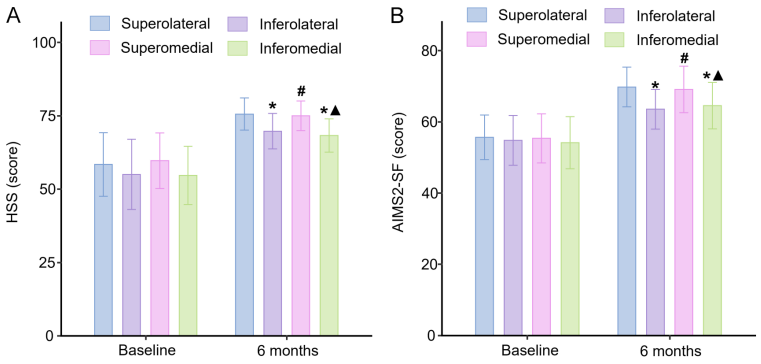

Figure 6. HSS and AIMS2-SF scores in different puncture-site groups. Note: *P<0.05 compared to the superolateral group; #P<0.05 compared to the inferolateral group; ▲P<0.05 compared to the superomedial group; A: HSS score; B: AIMS2-SF score.

inferolateral and inferomedial groups than in the superolateral and superomedial groups (P<0.05; **Figure 5**).

HSS and AIMS2-SF scores among puncture-site subgroups: After treatment, all groups demonstrated significant increases in HSS and AIMS2-SF scores (P<0.05). The superolateral and superomedial groups showed higher HSS and AIMS2-SF scores than the inferolateral and inferomedial groups (P<0.05; **Figure 6**).

Inflammatory markers among puncture-site subgroups: Serum levels of IL-1β, CRP, and TNF-α decreased significantly in all groups after treatment (P<0.05) and were lower in the superolateral and superomedial groups than in the inferolateral and inferomedial groups (P<0.05; **Figure 7**).

Adverse events: Among the four groups, a total of 7 patients experienced adverse events, with incidences of 3.85% in the superolateral group, 12.00% in the inferolateral group, 3.70% in the superomedial group, and 8.33% in the inferomedial group. No significant difference in incidence was seen (χ^2=1.859, P=0.582; **Figure 8**).

Discussion

Non-surgical management of KOA includes pharmacologic therapy and intra-articular interventions [11-14]. Among these options, sodium hyaluronate has been widely adopted due to its favorable safety profile and its ability to improve joint lubrication and pain [15, 16]. Previous studies have shown that its efficacy is comparable to that of other non-surgical treatments [17, 18]. Consistent with these findings, our results suggest that sodium hyaluronate may provide superior improvements in pain and function compared to triamcinolone acetonide over a 6-month period.

In the present study, treatment with sodium hyaluronate was associated with improvements in pain, joint function, and inflammatory markers, along with a lower incidence of adverse events compared to triamcinolone acetonide. These differences may reflect the distinct therapeutic mechanisms of the two agents. Sodium hyaluronate is a high-molecular-weight polysaccharide with a structure similar to endogenous hyaluronic acid in synovial fluid. It increases synovial fluid viscosity and lubrication, thereby reducing friction and wear of articular cartilage. In addition, sodium hyaluronate exerts anti-inflammatory effects by suppressing the release of inflammatory mediators and alleviating synovial inflammation [19, 20]. In contrast, triamcinolone acetonide mainly provides rapid pain relief through inhibition of inflammatory responses, but its effect is relatively short-lived, and repeated use may have adverse effects on articular cartilage [21, 22].

In clinical practice, intra-articular injection aims primarily to ensure accurate delivery of medication into the joint cavity. Although previous studies have suggested that lateral approaches may provide higher injection accuracy and fewer minor complications compared to medial approaches [23-26], the effect of puncture-site selection on clinical outcomes has been less thoroughly investigated. In the present study, sodium hyaluronate injection by the inferomedial approach was associated with greater pain relief, consistent with previous reports [27, 28], whereas the superolateral and superomedial approaches demonstrated greater improvements in joint stiffness, physical function, and quality of life. These findings suggest that puncture-site selection may influence both symptom relief and functional recovery.

Anatomic and physicochemical factors may partly explain these differences. Injection thr-

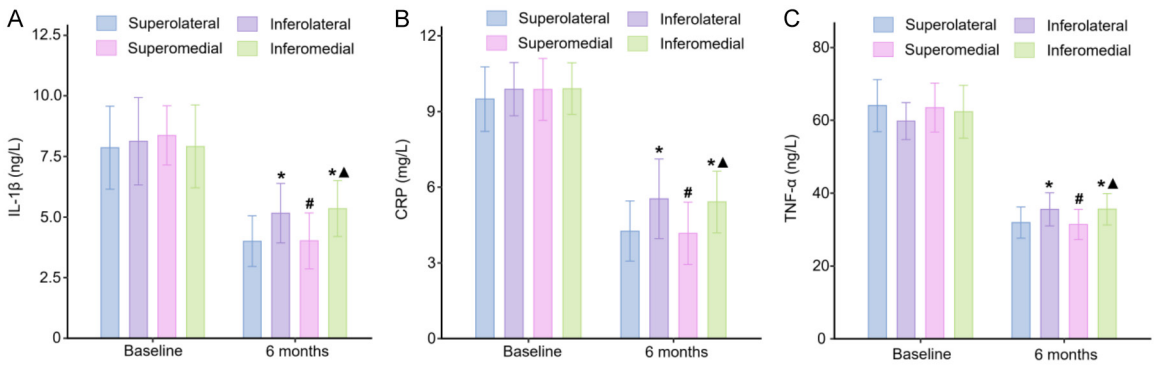

Figure 7. Inflammatory markers in different puncture-site groups. Note: *P<0.05 compared to the superolateral group; #P<0.05 compared to the inferolateral group; ▲P<0.05 compared to the superomedial group; A: IL-1β; B: CRP; C: TNF-α.

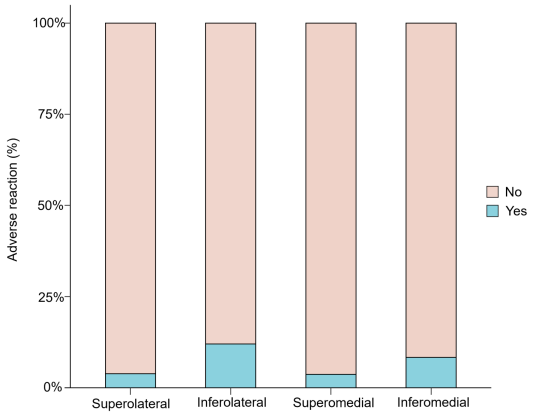

Figure 8. Adverse events in different puncture-site groups.

ough the inferomedial approach involves less soft tissue penetration and allows easier access to the joint cavity when the knee is flexed to 90°, which may result in less injection-related discomfort and an enhanced pain relief [29]. In the superolateral and superomedial techniques, the needle tip can contact bone, the quadriceps tendon, and suprapatellar synovium and cause further delay in the relief of pain [30]. Additionally, patients with KOA often have degeneration of patellofemoral cartilage. Injection through superior patellar routes, coupled with the high molecular weight and rheological properties of sodium hyaluronate, might enhance the coverage of patellofemoral lesions under the simultaneous influence of gravity and rheological behavior, improving joint lubrication and functional status [31-33]. Not directly assessed in this study were injection accuracy and intra-articular drug distribution, meaning careful interpretation of the above findings is required.

Sodium hyaluronate injection at superolateral and superomedial punctures led to reduced concentrations of IL-1β, IL-6, and TNF-α than at inferolateral and inferomedial punctures; hence, the anti-inflammatory actions are different by puncture site. Previous studies have shown that inflammatory mediators such as IL-1β, IL-6, TNF-α, and CRP worsen the progression of KOA by activating signaling pathways whereas MAPKs and Toll-like receptors which promote synovial inflammation, and lead to cartilage matrix damage [34]. Sodium hyaluronate helps in inhibition of the inflammatory process by inhibiting leukocyte chemotaxis and weakening cell interactions, leading to symptom improvement and slowing down of progression of the disease [35].

The limitations of this study are numerous. Initially, it was a single center retrospective study, which can introduce selection bias. The relatively smaller sample size of each puncture site subgroup limited the statistical power. Moreover, the related mechanisms need to be verified further, and we did not carry out any objective assessments of injection accuracy, or of intra-articular drug distribution. The duration of follow-up was short and long-term outcomes could not be evaluated. Further multicenter, prospective randomized controlled studies with imaging-based assessment of injection accuracy and longer follow-up periods are warranted to further clarify the long term effect and mechanism of different puncture sites in sodium hyaluronate treatment for KOA.

Conclusion

Intra-articular injection of sodium hyaluronate is effective and safe for the treatment of knee osteoarthritis. Clinical outcomes vary among different puncture sites. The inferomedial approach shows an advantage in pain relief, whereas the superolateral and superomedial approaches provide similar overall benefits in improving joint function, inflammatory response, and quality of life.

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Disclosure of conflict of interest

None.

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