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Original Article

Intra-articular sodium hyaluronate, compound betamethasone, and ropivacaine combined with arthroscopic debridement in patients with knee osteoarthritis

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Abstract: Objective: To evaluate the efficacy of sodium hyaluronate (SH), compound betamethasone (BT), and ropivacaine (Rop) in combination with arthroscopic debridement (AD) for the treatment of knee osteoarthritis (KOA). Methods: A retrospective analysis was conducted on 107 KOA patients treated at Shantou Central Hospital I, including 52 patients in the control group who received AD alone and 55 patients in the observation group who additionally received intra-articular SH, compound BT, and Rop. Treatment efficacy, pain levels, knee joint function, lower limb motor function, serum inflammatory markers, quality of life, and sleep quality were assessed and compared between the two groups. Univariate and multivariate logistic regression analyses were performed to identify factors influencing treatment outcomes. Results: The observation group showed significantly better outcomes than the control group in terms of overall treatment efficacy, pain relief, improvement in joint and lower limb function, reduction in inflammatory markers, and enhancement of both sleep quality and overall quality of life. Prolonged disease duration was identified as an independent risk factor for poor treatment outcomes. Conclusion: The combination of SH, compound BT, and Rop with AD offers significant clinical advantages in the management of KOA, supporting its broader adoption in clinical practice.

Keywords: Knee osteoarthritis, arthroscopic debridement, sodium hyaluronate, compound betamethasone, ropivacaine

Introduction

Knee osteoarthritis (KOA) is a prevalent degenerative and disabling peripheral joint disease, particularly common among older adults [1, 2]. It is the most frequent form of osteoarthritis, affecting up to 6% of the adult population, and prevalence increases with age [3]. Epidemiologic studies report a risk as high as 42.8% in elderly women and 21.5% in elderly men [4]. Clinically, KOA presents with knee pain, morning stiffness, reduced mobility, and in severe cases, disability - negatively affecting patients' daily lives and work [5].

Surgical intervention remains the primary treatment option for advanced KOA. Arthroscopic debridement (AD), a minimally invasive procedure, is commonly employed to treat degenerative changes in the knee. It effectively removes damaged cartilage and loose tissue while smoothing joint surfaces [6, 7]. However, postoperative swelling, pain, and other symptoms are common, necessitating adjunct pharmacologic interventions to improve therapeutic outcomes and promote recovery [8, 9].

Sodium hyaluronate (SH), a high-molecular-weight glucosamine secreted by chondrocytes, synoviocytes, and fibroblasts, plays a key role in maintaining joint viscoelasticity and lubrication [10]. In KOA patients, intra-articular SH levels are significantly reduced. Supplementation has been shown to repair cartilage damage, relieve pain, and reduce dependence on analgesics [11].

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Compound betamethasone (BT) is a combination of BT disodium phosphate and BT dipropionate, providing both rapid and sustained anti-inflammatory effects [12]. Liu et al. [13] demonstrated that compound BT cocktail therapy in patients undergoing unilateral unicompartmental knee arthroplasty (UKA) effectively relieved acute pain and improved knee function without increasing the risk of complications.

Ropivacaine (Rop), a widely used local anesthetic in surgeries such as general operations, arthroplasty, and cardiac procedures, offers rapid and sustained pain relief [14]. In total knee arthroplasty, Rop has been shown to provide effective analgesia while reducing postoperative morphine requirements [15, 16].

This study hypothesized that the combination of SH, compound BT, and Rop with AD may enhance treatment outcomes in KOA patients. To test this, we conducted a retrospective analysis and present the results herein. This study offers several key innovations: (1) It was the first to evaluate the combined application of SH, compound BT, and Rop in AD for KOA; (2) It provided a comprehensive assessment of clinical outcomes - including therapeutic efficacy, pain relief, joint and limb function, inflammatory biomarkers, quality of life, and sleep quality - demonstrating the clinical value of this novel combination therapy in improving recovery and optimizing treatment strategies for KOA.

Materials and methods

General data

This retrospective study was approved by the Ethics Committee of Shantou Central Hospital. Clinical data were collected from 107 KOA patients admitted to Shantou Central Hospital between February 2020 and April 2023. Among them, 52 patients comprised the control group and received AD alone, while 55 patients in the observation group received additional intra-articular injections of SH, compound BT, and Rop.

Inclusion criteria were as follows: diagnosed KOA; no contraindications to the treatment plan; Kellgren-Lawrence (K-L) grade I-II on radiographic imaging; no recent knee trauma, surgery, or infection; age between 18 and 80 years; symptom duration ≥ 3 months; failure of conservative treatments (e.g., medication, physiotherapy) for ≥ 6 weeks; and complete medical records.

Exclusion criteria included: known allergy or hypersensitivity to study drugs; significant joint deformities (e.g., varus/valgus deformity, knee flexion contracture, congenital meniscal dysplasia, or post-traumatic limitations); comorbid conditions (e.g., knee tumors, rheumatoid or rheumatic arthritis, or lumbar/hip joint disease evident on imaging); local contraindications (e.g., skin infection or soft tissue damage at injection site); recent use of corticosteroids or intra-articular injections within 3 months; severe systemic conditions (e.g., cardiovascular, pulmonary, hepatic, or renal insufficiency); uncontrolled diabetes, active peptic ulcers, severe osteoporosis; pregnancy or lactation; psychiatric illness or cognitive impairment; or pre-existing sleep disorders.

Treatment methods

The control group underwent standard AD. Under epidural anesthesia, patients were placed in the supine position with a tourniquet applied to the thigh base. Normal saline (Shanghai Yaji Biotechnology Co., Ltd., HBPT033) was infused into the suprapatellar pouch by a perfusion system. Arthroscopic access was established through the medial and lateral infrapatellar portals. The patellofemoral joint, suprapatellar bursa, and medial/lateral compartments were examined. Necrotic, hyperplastic, and damaged cartilage, as well as hypertrophic synovium, were debrided. Meniscal repair and removal of free bodies were also performed. The joint cavity was thoroughly irrigated and drained.

In the observation group, patients received the same AD procedure followed by intra-articular injections. After aspirating synovial fluid, a mixture of SH (2.5 mL; Shanghai Yiji Industrial Co., Ltd., YJ-P226899), compound BT (1.0 mL; Sichuan Weikeqi Biotechnology Co., Ltd., WKQ-0002505), and Rop (20.0 mL; Shanghai China Wines Da Industrial Co., Ltd., HY-B0563A) was injected into the joint cavity once weekly for five weeks.

Endpoints

Treatment outcomes were classified into four categories: Excellent: Complete resolution of symptoms and restoration of knee function.

Table 1. Comparison of General information

Factor	Control group (n=52)	Observation group (n=55)	χ^2/t	P
Age (years)	47.00±6.80	45.44±7.75	1.104	0.272
Sex			1.505	0.220
Male	25 (48.08)	20 (36.36)		
Female	27 (51.92)	35 (63.64)		
Disease duration (months)	34.17±5.59	34.38±5.68	0.193	0.848
BMI (kg/m^2)	23.38±3.85	23.24±3.60	0.194	0.846
K-L radiological classification			0.242	0.623
I	24 (46.15)	28 (50.91)		
II	28 (53.85)	27 (49.09)		
Family disease history			0.846	0.358
Yes	10 (19.23)	7 (12.73)		
No	42 (80.77)	48 (87.27)		

Notes: BMI, body mass index; K-L, Kellgren-Lawrence.

Table 2. Comparison of treatment outcomes

Rating	Control group (n=52)	Observation group (n=55)	χ^2	P
Excellent	14 (26.92)	22 (40.00)		
Good	23 (44.23)	27 (49.09)		
Fair	10 (19.23)	3 (5.45)		
Poor	5 (9.62)	3 (5.45)		
Excellent and good rate	37 (71.15)	49 (89.09)	5.452	0.020

Good: Marked improvement in symptoms and near-normal knee function. Fair: Symptom relief with partial functional recovery. Poor: No improvement or worsening of condition. The excellent and good rate was calculated as: (excellent + good cases)/total cases.

Pain intensity was assessed using the Visual Analogue Scale (VAS, 0-10), with higher scores indicating greater pain.

Knee Joint Function was evaluated using the Lysholm Score (range: 0-100) and the Hospital for Special Surgery (HSS) knee score (range: 0-80), with higher scores indicating better function.

Lower extremity motor function was assessed using the lower-limb Fugl-Meyer Assessment (FMA; range: 0-34) and the Western Ontario and McMaster Universities Osteoarthritis Index (WOMAC; range: 0-96). Higher FMA scores indicate better motor function, while higher WOMAC scores reflect more severe pain and functional limitation.

Blood samples (3 mL) were collected from fasting patients before and after treatment. After centrifugation, serum levels of C-reactive protein (CRP), tumor necrosis factor-alpha (TNF-α), and interleukin-6 (IL-6) were quantified using enzyme-linked immunosorbent assay (ELISA; AmyJet Scientific Inc., NDC-KBB-8W0-P34-5 x 96, NDC-KSP-BU8T-G5-96, NDC-KBB-J55224-96).

Quality of lifewas assessed using the Short Form-36 (SF-36), with higher scores (range: 0-100) indicating better quality of life.

Sleep quality was evaluated using the Pittsburgh Sleep Quality Index (PSQI), a validated 19-item questionnaire covering seven domains. Each domain is scored from 0 to 3, with higher total scores (range: 0-21) indicating poorer sleep quality.

Primary endpoints included treatment outcomes, pain level, knee joint function, lower extremity motor function, and serum inflammatory markers. Secondary endpoints comprised quality of life and sleep quality.

Statistical analysis

Measureed data were presented as mean ± SEM. Between-group comparisons were conducted using the independent samples t-test, while within-group comparisons used the paired t-test. Categorical data were expressed as frequencies and percentages, with intergroup comparisons conducted using the χ^2 test. Statistical analyses were performed using SPSS 22.0, and *p*-values <0.05 were considered statistically significant.

Results

Comparison of general data

There were no significant differences between the observation and control groups in terms of

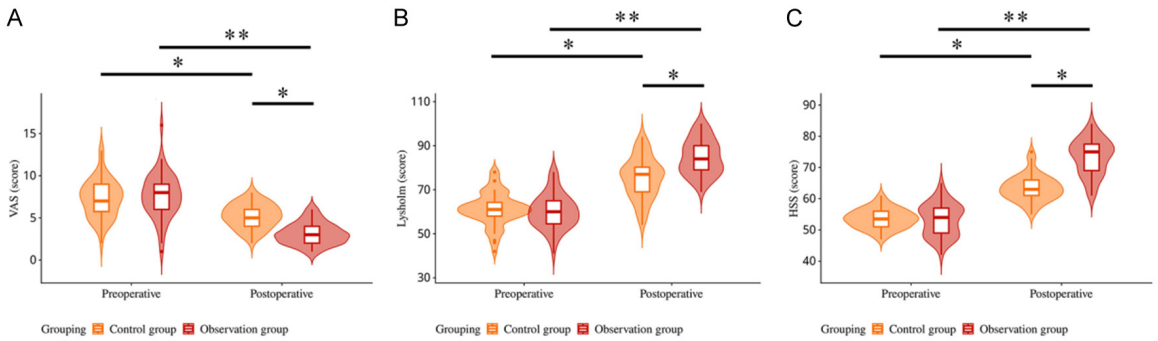

Figure 1. Comparison of VAS, Lysholm, and HSS scores. A. Pre- and post-operative VAS scores in both groups. B. Pre- and post-operative Lysholm scores in both groups. C. Pre- and post-operative HSS scores in both groups. Notes: VAS, Visual Analogue Scale; HSS, Hospital for Special Surgery. *P<0.05, **P<0.01.

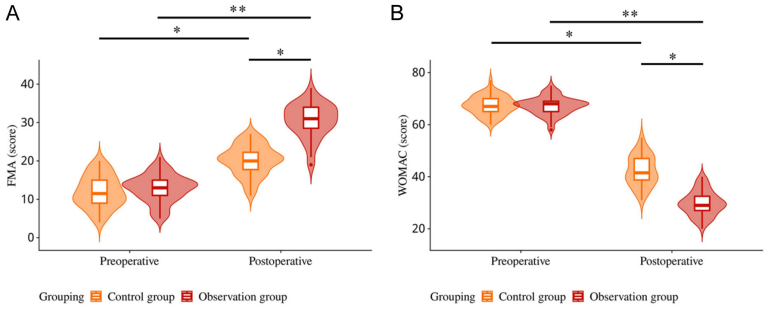

Figure 2. Comparison of FMA and WOMAC scores. A. Pre- and post-operative FMA scores in both groups. B. Pre- and post-operative WOMAC scores in both groups. Notes: FMA, Fugl-Meyer Motor Assessment; WOMAC, Western Ontario and McMaster Universities Osteoarthritis Index. *P<0.05, **P<0.01.

age, sex, disease duration, body mass index (BMI), K-L radiographic classification, family history of disease, or other baseline characteristics (all P>0.05). See **Table 1**.

Comparison of treatment outcomes

The number of patients rated as having excellent or good outcomes was 37 in the control group and 49 in the observation group, with a significantly higher excellent and good rate in the observation group compared to the control group (89.09% vs. 71.15%; P<0.05). See **Table 2**.

Comparison of VAS, Lysholm, and HSS scores

Preoperative VAS, Lysholm, and HSS scores were comparable between groups (all P>0.05). After treatment, VAS scores decreased significantly, while Lysholm and HSS scores increased significantly in both groups. The observation group showed greater improvements, with lower VAS and higher Lysholm and HSS scores than the control group (all P<0.05). See **Figure 1**.

Comparison of FMA and WOMAC scores

There were no significant differences in FMA and WOMAC scores between groups before treatment (both P>0.05). Following treatment, FMA scores increased and WOMAC scores decreased significantly in both groups, with the observation group achieving better outcomes than the control group (both P<0.05). See **Figure 2**.

Comparison of serum inflammatory markers

Baseline serum levels of CRP, TNF-α and IL-6 did not differ significantly between groups (all P>0.05). Post-treatment levels of all three markers decreased significantly in both groups, with more pronounced reductions observed in the observation group (all P<0.05). See **Figure 3**.

Comparison of SF-36 scores

Pre-treatment SF-36 scores were similar between the two groups (P>0.05). After treatment, SF-36 scores significantly increased in both groups, with the observation group showing greater improvements than the control group (P<0.05). See **Figure 4**.

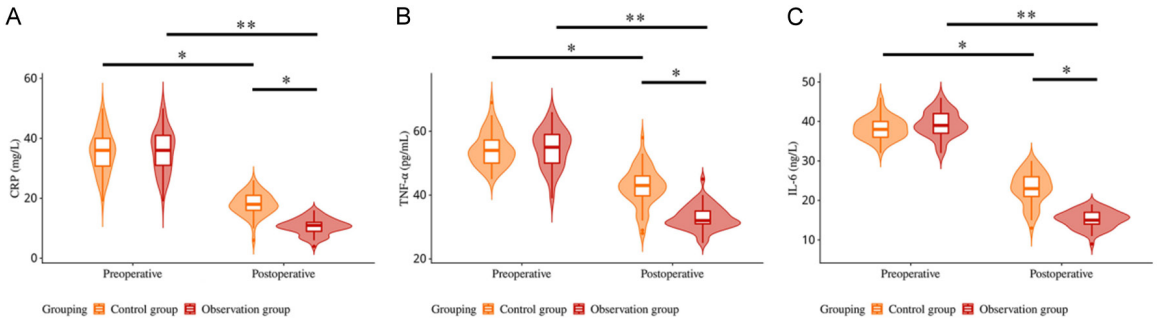

Figure 3. Comparison of serum inflammation markers. A. Pre- and post-operative CRP in both groups. B. Pre- and post-operative TNF-α in both groups. C. Pre- and post-operative IL-6 in both groups. Notes: CRP, C-reactive protein; TNF-α, tumor necrosis factor-α; IL-6, interleukin 6. *P<0.05, **P<0.01.

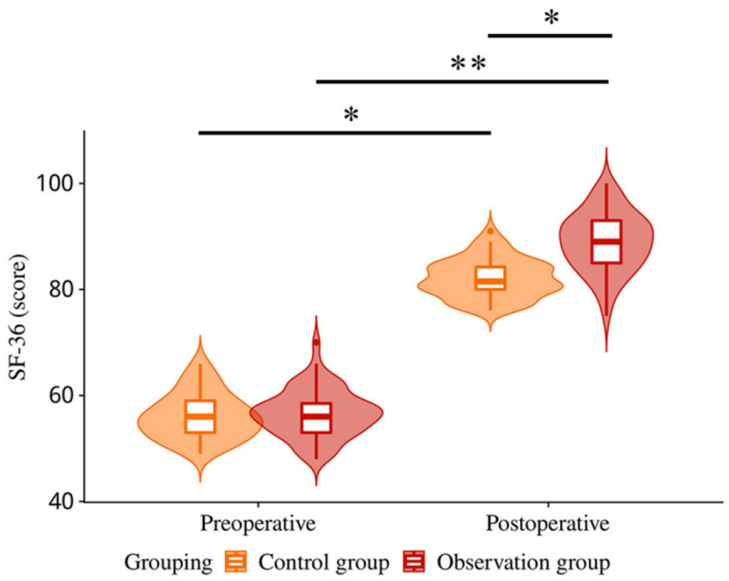

Figure 4. Comparison of SF-36 scores. Note: SF-36, Short-Form 36 Item Health Survey. *P<0.05, **P<0.01.

Table 3. Comparison of Post-intervention PSQI in two groups

Domain	Control group (n=52)	Observation group (n=55)	t	P
Sleep quality	1.40±0.53	1.15±0.45	2.635	0.010
Sleep latency	1.31±0.64	1.04±0.51	2.420	0.017
Sleep efficiency	1.40±0.69	1.09±0.44	2.787	0.006
Sleep duration	1.50±0.64	1.24±0.54	2.276	0.025
Sleep disturbances	1.15±0.75	0.82±0.47	2.743	0.007
Daytime dysfunction	1.50±0.54	1.15±0.59	3.196	0.002
Sleep medications	1.33±0.81	0.65±0.55	5.105	<0.001

Note: PSQI, Pittsburgh Sleep Quality Index.

Comparison of sleep quality

Post-treatment PSQI domain scores were significantly lower across all seven domains in the observation group compared to the control group (all P<0.05). See **Table 3**.

Risk factors influencing treatment outcomes

Univariate analysis identified age, disease duration, K-L radiographic classification, and treatment modality as factors significantly associated with treatment efficacy (P<0.05). Gender, BMI, and family history showed no significant correlations (all P>0.05).

Multivariate logistic regression further revealed that longer disease duration was an independent risk factor for poor treatment outcomes (P=0.044), while age, K-L classification, and treatment modality were not significant predictors (all P>0.05). See **Tables 4** and **5**.

Discussion

As a chronic and currently incurable cartilage disorder, knee osteoarthritis (KOA) is best managed through early prevention and timely intervention [17, 18]. AD has been shown to alleviate symptoms and delay the need for further surgical intervention in elderly KOA patients [19]. This study aimed to optimize AD by integrating pharmacologic adjuncts, providing a novel approach to KOA management.

Table 4. Univariate analysis of factors influencing patient treatment outcomes

Factor	Non-excellent-or-good group (n=21)	Excellent-and-good group (n=86)	χ^2	P
Age (years)			4.681	0.031
<45 (n=48)	5 (23.81)	43 (50.00)		
≥45 (n=59)	16 (76.19)	43 (50.00)		
Gender			2.770	0.096
Male (n=45)	12 (57.14)	32 (37.21)		
Female (n=63)	9 (42.86)	54 (62.79)		
Disease duration (months)			4.586	0.032
<35 (n=58)	7 (33.33)	51 (59.30)		
≥35 (n=49)	14 (66.67)	35 (40.70)		
BMI (kg/m^2)			1.600	0.206
<24 (n=54)	8 (38.10)	46 (53.49)		
≥24 (n=53)	13 (61.90)	40 (46.51)		
K-L radiological classification			4.195	0.041
I (n=52)	6 (28.57)	46 (53.49)		
II (n=55)	15 (71.43)	40 (46.51)		
Family disease history			0.050	0.823
Yes (n=17)	3 (14.29)	14 (16.28)		
No (n=90)	18 (85.71)	72 (83.72)		
Treatment modality			5.452	0.020
Arthroscopic debridement (n=52)	15 (71.43)	37 (43.02)		
Arthroscopic debridement + sodium hyaluronate + compound betamethasone + ropivacaine (n=55)	6 (28.57)	49 (56.98)		

Notes: BMI, body mass index; K-L, Kellgren-Lawrence.

Table 5. Multivariate analysis of factors influencing patient treatment outcomes

Factor	B	Standard error	Wald	P	Exp (B)	95% CI
Age (years)	0.892	0.591	2.281	0.131	2.440	0.767-7.762
Disease duration (months)	1.095	0.545	4.041	0.044	2.988	1.028-8.688
K-L radiological classification	0.984	0.564	3.051	0.081	2.676	0.887-8.077
Treatment modality	1.059	0.558	3.602	0.058	2.883	0.966-8.605

Notes: K-L, Kellgren-Lawrence.

In terms of clinical symptom relief and knee function recovery, the observation group achieved an excellent and good rate of 89.09%, significantly higher than the 71.15% observed in the control group. This suggests that the combination of SH, compound BT, and Rop with AD enhances therapeutic efficacy in KOA. The improvement may be attributed to intra-articular irritation caused by AD, which can trigger postoperative exudation and inflammatory responses that delay recovery [20, 21]. SH, compound BT, and Rop may act synergistically to accelerate functional recovery from different mechanistic perspectives. Specifically, SH contributes to joint lubrication and cartilage protection, thereby slowing disease progression [22, 23]. Compound BT exerts anti-inflammatory effects and may prevent early-stage KOA progression by downregulating the mRNA expression of matrix metalloproteinase-13 (MMP-13) and ADAMTS9 [24]. Rop, as part of an intra-articular cocktail, has also been shown to inhibit cartilage degradation and inflammatory mediator secretion by downregulating MMP-7 and MMP-8 [25].

Postoperative improvements in VAS, Lysholm, and HSS scores further support the analgesic and functional benefits of the combination therapy. Additionally, more significantly

enhanced FMA and reduced WOMAC scores in the observation group reflect better lower-limb motor function recovery. The observed reductions in CRP, TNF-α, and IL-6 levels in the observation group confirm the anti-inflammatory effects of the combined treatment. Elevated CRP is associated with joint tissue damage; high TNF-α levels can promote synovial fibrosis and cartilage lesions; and increased IL-6 is implicated in osteoclast-mediated cartilage destruction [26-28]. Supporting evidence includes the anti-inflammatory effect of SH derivatives in KOA [29], TNF-α inhibition by compound BT in psoriasis [30], and reductions in TNF-α and IL-6 levels by Rop in rat models of fecal peritonitis [31].

Moreover, significant improvements in SF-36 scores in the observation group indicate a notable enhancement in overall quality of life. The treatment also demonstrated superior efficacy in improving sleep quality, with significant improvements across all PSQI domains compared to conventional treatment.

Univariate analysis identified age, disease duration, K-L classification, and treatment modality as factors influencing treatment efficacy. Multivariate logistic regression revealed that disease duration ≥ 35 months was an independent risk factor for treatment failure. This finding underscores the importance of early diagnosis and intervention, as prolonged disease course is often accompanied by severe cartilage degeneration and structural joint changes, reducing the efficacy of therapeutic interventions.

Several limitations should be acknowledged. First, the absence of SF-36 subscale analysis limits our ability to evaluate domain-specific quality-of-life outcomes. Future studies should incorporate detailed subdomain assessments. Second, the current risk prediction model remains unvalidated; increasing the sample size in future research will enable more robust model evaluation and refinement. Lastly, the single-factor analysis design did not support the development of a clinically applicable nomogram. Future research should explore multifactorial modeling approaches to facilitate the construction of predictive tools for clinical application.

In summary, the combination of SH, compound BT, and Rop with AD demonstrated significant therapeutic benefits in KOA management. This multimodal intervention effectively relieved clinical symptoms and pain, enhances knee joint and lower-limb function, reduced systemic inflammation, and improved quality of life and sleep. Importantly, our findings highlight prolonged disease duration as an independent predictor of poor treatment outcomes, emphasizing the need for early and proactive therapeutic strategies.

Disclosure of conflict of interest

None.

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