

The Outcome of Intra Articular Ketorolac vs Corticosteroid Injection in Symptomatic Knee Osteoarthritis

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Abstract:**Background:** Intra-articular (IA) therapy is widely used for symptomatic knee osteoarthritis (OA) when oral medications are inadequate or poorly tolerated. This randomized controlled study compared the efficacy of IA ketorolac versus methylprednisolone acetate in relieving pain and improving function in patients with symptomatic knee OA.**Methods:** One hundred and twelve adults with clinically and radiographically confirmed knee OA were randomized to receive a single IA injection of either ketorolac (30 mg with lignocaine) or methylprednisolone acetate (80 mg with lignocaine). Pain was assessed using the Visual Analogue Scale (VAS) and function using the Oxford Knee Score (OKS) at baseline, 4 weeks and 12 weeks.**Results:** Baseline characteristics and scores were comparable between groups. Mean VAS decreased from 7.0 to 5.3 and 4.7 at 4 and 12 weeks in the ketorolac group, and from 7.2 to 3.5 and 1.6 in the corticosteroid group. Between-group analysis showed significantly lower VAS with corticosteroid at 4 weeks (mean difference 1.8, $p < 0.01$) and 12 weeks (mean difference 3.1, $p < 0.01$). OKS improved significantly in both groups, with consistently superior gains in the corticosteroid arm.**Conclusions:** Both IA ketorolac and methylprednisolone improved symptoms, but corticosteroid produced greater and more sustained pain relief and functional benefit.**Keywords:** Knee osteoarthritis, Intra-articular injection, Corticosteroid, Ketorolac, Pain management.**DOI:** 10.25258/ijcpr.18.3.231

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Introduction

Osteoarthritis (OA) is one of the most common disabling joint disorders worldwide and represents a major cause of chronic pain, functional limitation and disability. Knee OA, in particular, is highly prevalent because the knee is a major weight-bearing joint that is frequently subjected to mechanical load, trauma and overuse. The disease is characterized by progressive degeneration of articular cartilage, variable synovial inflammation, and structural changes in subchondral bone, ultimately resulting in pain, stiffness, joint deformity and impaired quality of life.

Multiple risk factors contribute to the development and progression of knee OA, including advancing age, female sex, obesity, prior joint injury, adverse occupational loading and anatomical malalignment. [6–10] The prevalence of symptomatic knee OA increases markedly after 50 years of age and is higher among women than men. Epidemiological studies from Asian populations, including India and

China, have reported high rates of knee pain and radiographic OA, particularly in rural settings where heavy physical work, poorer nutrition and lower socioeconomic status are common.

The clinical diagnosis of knee OA relies on typical symptoms—usage-related knee pain, stiffness and reduced function—combined with physical signs such as joint line tenderness, crepitus, bony enlargement, deformity and limited range of motion. Radiographic assessment using the Kellgren–Lawrence grading system (grades 0–4) remains the standard imaging tool in clinical practice, although radiographic changes correlate imperfectly with symptoms. Management aims to alleviate pain, preserve or improve function, slow structural progression and delay or avoid total knee arthroplasty (TKA).

Non-pharmacological measures—including patient education, weight reduction, exercise therapy, bracing and assistive devices—form the cornerstone

of initial management. Pharmacological options range from paracetamol and nonsteroidal anti-inflammatory drugs (NSAIDs) to opioids and symptomatic slow-acting drugs; however, systemic therapy may be limited by gastrointestinal, renal and cardiovascular adverse effects, particularly in older patients. When conservative oral measures are insufficient or poorly tolerated, intra-articular (IA) therapies such as corticosteroids, hyaluronic acid (HA) and platelet-rich plasma (PRP) are widely used to provide local pain relief and functional improvement.

Intra-articular corticosteroid injections produce pain relief predominantly through potent local anti-inflammatory and immunomodulatory actions, including suppression of cytokine production, inhibition of inflammatory cell migration and reduction of vascular permeability. They are effective for short-term symptom control during OA flare-ups, especially when joint effusion and synovitis are present. However, repeated IA steroid administration has been associated, in some experimental and clinical reports, with acceleration of cartilage degeneration, alteration of articular cartilage mechanical properties and increased risk of joint infection. [3,17–19]

Several comparative studies have assessed IA ketorolac versus corticosteroids in knee OA, reporting that both agents improve pain and function, with some suggesting comparable short-term efficacy and others indicating slightly more durable benefit with corticosteroids.[22–27] Nonetheless, data remain limited, and most prior trials have used triamcinolone, often in multiple weekly injections and frequently in combination with HA.[22–27] Evidence directly comparing single-dose intra-articular ketorolac with methylprednisolone acetate without adjunctive HA is scarce. The present prospective randomized controlled study was therefore undertaken to compare the analgesic and functional outcomes of single IA injections of ketorolac versus methylprednisolone acetate in patients with symptomatic knee OA.

Methodology

Study design and setting: This was a prospective randomized controlled clinical study conducted in the Department of Orthopaedics, over 18 months from 1 May 2022 to 31 October 2024. The study protocol was approved by the Institutional Ethics Committee and conformed to the principles of the Declaration of Helsinki. Written informed consent was obtained from all participants prior to enrolment.

Study population: Eligible participants were adults aged 40–85 years with symptomatic primary knee

OA diagnosed clinically and radiographically by the treating orthopaedic surgeon.

Key inclusion criteria were:

- Age 40–85 years.
- Symptomatic OA of the knee joint with pain and functional limitation.

Exclusion criteria included:

- History of recent knee trauma.
- Previous joint infection or local site infection.
- Inflammatory arthritis or autoimmune disease.
- Malignancy.
- Known allergy to NSAIDs or corticosteroids.
- Significant renal disease precluding NSAID use.
- Prior IA injection in the index knee within the preceding 6 months.
- Uncontrolled diabetes mellitus.

Sample size and randomization

Sample size was calculated using the formula:

$$n = (Z_{\alpha/2} + Z_{\beta})^2 \times 2 \times SD^2 / d^2$$

where $Z_{\alpha/2} = 3.29$ (two-sided alpha 0.001), $Z_{\beta} = 1.64$ (power 95%), SD was the pooled standard deviation of VAS at 3 months from Verma et al., and d was the clinically relevant difference in mean VAS between groups. Using reported mean VAS values at 3 months for triamcinolone (2.24 ± 0.14) and ketorolac (2.48 ± 0.35), the required sample size per group was estimated as 50, which was increased by 10% to 55 to account for potential loss to follow-up. Consecutive patients fulfilling eligibility criteria were recruited and randomized into two groups (ketorolac or corticosteroid) using a simple lottery method. A total of 120 chits were prepared (60 labelled “corticosteroid” and 60 labelled “ketorolac”) to achieve nearly equal allocation; 57 patients were ultimately assigned to the ketorolac group and 55 to the corticosteroid group. The treating clinician was not blinded to group allocation, but outcome measures (VAS and OKS) were patient-reported.

Interventions

All procedures were performed in the outpatient procedure room under strict aseptic precautions.

- **Ketorolac group:** Patients received a single intra-articular injection consisting of 5 ml of 2% lignocaine plus 1 ml containing 30 mg ketorolac.
- **Corticosteroid group:** Patients received a single intra-articular injection consisting of 5 ml of 2% lignocaine plus 2 ml containing 80 mg methylprednisolone acetate.

The skin around the knee was prepared with povidone-iodine, and injections were administered

using standard landmark-guided technique into the knee joint. After injection, patients were observed for 15 minutes for immediate adverse reactions, counselled regarding post-procedure care, and discharged with instructions for local ice application, knee range-of-motion exercises and regular physiotherapy. Oral paracetamol 650 mg was permitted as rescue analgesia.

Data were collected using a pre-designed proforma by the surgeon. Baseline variables included:

- Demographics: age and sex.
- Clinical details: side involved, presenting complaints and examination findings.
- Type of IA injection received.

Outcome measures were:

1. **Pain:** Assessed using a 10-point Visual Analogue Scale (VAS; 0 = no pain, 10 = worst possible pain).
2. **Functional outcome:** Assessed using the Oxford Knee Score (OKS), a 12-item patient-reported questionnaire that evaluates pain and function.

The original English OKS was translated into Hindi following a standard forward-backward translation process by physiotherapists and professional language experts, with subsequent pretesting in 20 patients to ensure clarity and cultural appropriateness. The Hindi version (OKS-Hindi) has been previously validated in Indian patients with knee OA.

Both VAS and OKS were recorded at three time points:

- Baseline (time of injection).
- 4 weeks post-injection.
- 12 weeks post-injection.

Statistical analysis

Data were analysed using SPSS software version 24.0. Continuous variables were summarized as mean \pm standard deviation (SD), and categorical variables as frequencies and percentages. Within-group changes in VAS and OKS between baseline and follow-up visits were assessed using paired t-tests. Between-group comparisons of mean VAS and OKS at each time point were performed using independent samples t-tests. Associations between categorical variables (e.g. age group, sex, side affected) and treatment group were evaluated using chi-square tests. A p value < 0.05 was considered statistically significant.

Results

Participant flow and baseline characteristics

A total of 112 patients with symptomatic knee OA were enrolled. Of these, 57 were allocated to the ketorolac group and 55 to the corticosteroid group. Three patients in the ketorolac group and two in the corticosteroid group were lost to follow-up, leaving 54 and 53 patients, respectively, for final analysis (n = 107).

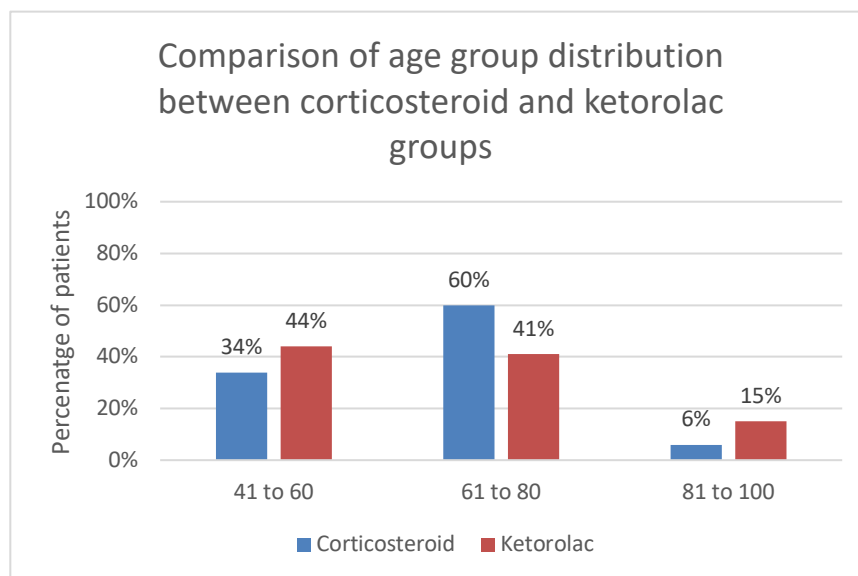


Figure 1: Comparison of age group distribution between corticosteroid and ketorolac groups

Half of all patients (50%) were aged 61–80 years, 39% were 41–60 years, and 10% were over 80 years. The mean age in the corticosteroid group was 66.2 ± 10.5 years compared with 64.1 ± 12.1 years in the ketorolac group ($p = 0.34$), indicating no significant

age difference between groups. Females comprised 66% of the corticosteroid group and 74% of the ketorolac group ($p = 0.36$). Overall, 70% of the study cohort were female. The left knee was affected in 53% of corticosteroid patients and 54% of ketorolac

patients ($p = 0.92$), indicating similar side distribution.

Within-group changes in pain and function: In the ketorolac group, mean baseline VAS was 7.0 ± 0.9 . This decreased significantly to 5.3 ± 0.8 at 4 weeks (mean difference 1.7, $p < 0.01$) and further to

4.7 ± 1.0 at 12 weeks (mean difference from baseline 2.3, $p < 0.01$). Correspondingly, mean OKS improved from 24.9 ± 4.6 at baseline to 32.0 ± 3.2 at 4 weeks (mean difference -7.1 , $p < 0.01$) and 34.9 ± 3.3 at 12 weeks (mean difference -10.0 , $p < 0.01$), indicating significant functional gains over time.

Table 1: Comparison of mean VAS at the time of injection, at 4 weeks and at 12 weeks in the ketorolac study group

Timepoint	N	Mean VAS in Ketorolac group	SD	Mean diff	p value*
At the time of injection	54	7.0	0.9	1.7	< 0.01
At 4 weeks	54	5.3	0.8		
At the time of injection	54	7.0	0.9	2.3	< 0.01
At 12 weeks	54	4.7	1.0		

*analyzed using paired t test

In the corticosteroid group, mean baseline VAS was 7.2 ± 0.8 . It declined significantly to 3.5 ± 0.6 at 4 weeks (mean difference 3.7, $p < 0.01$) and to 1.6 ± 0.5 at 12 weeks (mean difference 5.6, $p < 0.01$). Mean OKS increased from 25.0 ± 5.2 at baseline to 36.2 ± 3.4 at 4 weeks (mean difference -11.2 , $p <$

0.01) and to 43.1 ± 1.7 at 12 weeks (mean difference -18.1 , $p < 0.01$). Thus, both interventions produced statistically significant and clinically meaningful reductions in pain and improvements in function over 12 weeks.

Table 2: Comparison of mean VAS at the time of injection, at 4 weeks and at 12 weeks in the corticosteroid study group

Timepoint	N	Mean VAS in corticosteroid group	SD	Mean diff	p value*
At the time of injection	53	7.2	0.8	3.7	< 0.01
At 4 weeks	53	3.5	0.6		
At the time of injection	53	7.2	0.8	5.6	< 0.01
At 12 weeks	53	1.6	0.5		

*analysed using paired t test

Between-group comparisons: At baseline, there were no significant differences between groups in mean VAS (7.0 ± 0.9 ketorolac vs 7.2 ± 0.8 corticosteroid; $p = 0.25$) or mean OKS (24.9 ± 4.6 vs 25.0 ± 5.2 ; $p = 0.89$). This indicates successful randomization and comparability at study entry.

At 4 weeks, mean VAS was significantly lower in the corticosteroid group than in the ketorolac group (3.5 ± 0.6 vs 5.3 ± 0.8 ; mean difference 1.8; $p < 0.01$). At 12 weeks, this difference widened, with mean VAS of 1.6 ± 0.5 in the corticosteroid group compared to 4.7 ± 1.0 in the ketorolac group (mean difference 3.1; $p < 0.01$).

Table 3: Comparison of mean VAS between corticosteroid and ketorolac groups at the time of injection, at 4 weeks and at 12 weeks

Timepoint	Group	N	Mean VAS	SD	Mean diff	p value*
At the time of injection	Ketorolac	54	7.0	0.9	-0.2	0.25
	Corticosteroid	53	7.2	0.8		
At 4 weeks	Ketorolac	54	5.3	0.8	1.8	< 0.01
	Corticosteroid	53	3.5	0.6		
At 12 weeks	Ketorolac	54	4.7	1.0	3.1	< 0.01
	Corticosteroid	53	1.6	0.5		

*analyzed using independent t test

Similarly, functional outcomes favored corticosteroids. At 4 weeks, mean OKS was 36.2 ± 3.4 in the corticosteroid group vs 32.0 ± 3.2 in the ketorolac group (mean difference 4.2; $p < 0.01$). At 12 weeks, mean OKS was 43.1 ± 1.7 vs 34.9 ± 3.3 , respectively (mean difference 8.2; $p < 0.01$). These findings demonstrate superior pain relief and functional improvement with methylprednisolone

compared with ketorolac at both early and intermediate follow-up.

Adverse events: No major complications such as septic arthritis, severe bleeding, or persistent joint dysfunction were observed in either group during the study period. A few patients reported transient increase in knee pain after injection, which resolved spontaneously within 48–72 hours without

additional intervention. No cases of clinically apparent cartilage injury or systemic NSAID-related adverse events were documented, although imaging or laboratory surveillance for subclinical toxicity was not performed.

Discussion

This prospective randomized controlled study demonstrates that both intra-articular ketorolac and methylprednisolone acetate provide significant pain relief and functional improvement in patients with symptomatic knee OA over a 12-week period, but methylprednisolone achieves greater and more sustained benefit. Baseline demographic characteristics, pain and function scores were comparable between groups, supporting the validity of the between-group comparisons.

In the ketorolac group, VAS decreased by approximately 2.3 points and OKS increased by about 10 points at 12 weeks, indicating clinically relevant improvement. In contrast, the corticosteroid group experienced a reduction in VAS of 5.6 points and an 18-point increase in OKS over the same interval, with significantly better scores at both 4 and 12 weeks. These results suggest that, while ketorolac is effective, methylprednisolone injection confers superior analgesia and functional gain in the short to intermediate term following a single intra-articular dose.

Our findings are broadly consistent with existing literature evaluating IA corticosteroids and ketorolac in knee OA. Systematic reviews and meta-analyses have established that IA corticosteroids provide significant short-term pain relief (up to 4–6 weeks), though the benefit tends to diminish over longer follow-up. Najm et al. reported that corticosteroids showed a trend toward superiority over control in the short term, with diminishing advantage in the medium and long term. In the present study, the superiority of methylprednisolone persisted at 12 weeks, which may reflect the relatively high depot dose (80 mg), differences in patient characteristics, or the absence of concomitant HA or other injectables.

Evidence on intra-articular ketorolac in OA is more limited but generally supports its safety and efficacy. Bayat et al. compared single IA injections of ketorolac (30 mg) and triamcinolone (40 mg) in 38 patients with knee OA and found that both treatments reduced pain, stiffness and improved WOMAC and Lequesne scores, with triamcinolone showing greater pain reduction at 1 month but similar efficacy by 3 months. Xu et al. studied ketorolac versus corticosteroid, each combined with HA in a series of five weekly injections, and reported comparable improvements in VAS and WOMAC scores at 3 months, with no significant differences in treatment success rates. Jurgensmeier

et al. observed that IA ketorolac and triamcinolone produced similar improvements in hip and knee OA symptoms, with slightly more durable effects in the triamcinolone group for knees. Gondal et al. also reported no significant differences in VAS or WOMAC scores between ketorolac and triamcinolone at 1 week, 1 month and 3 months.

Unlike many of these studies, our trial used a single injection of ketorolac or methylprednisolone without HA supplementation and specifically compared methylprednisolone, a depot corticosteroid with relatively low solubility. [22–27] The more prolonged pain relief observed with methylprednisolone may be related to its depot formulation, which allows sustained intra-articular presence and continued local anti-inflammatory action. Ketorolac, being more soluble, might be cleared from the joint more rapidly, explaining the smaller magnitude of improvement at 12 weeks despite initial benefit.

The safety profile observed in this study is reassuring. No serious adverse events were recorded in either group, and only self-limiting post-injection pain was reported in a minority of patients. Prior work suggests that short-term IA ketorolac is generally safe, with gastrointestinal, renal and hematologic adverse effects being rare at such localized doses. Nonetheless, the long-term structural effects of repeated IA ketorolac on cartilage and subchondral bone remain insufficiently characterized, as do those of repeated corticosteroid injections, which have been associated with concerns of chondral toxicity in experimental models. [4,17–19] Importantly, our study only assessed clinical outcomes up to 12 weeks after a single injection, and did not evaluate radiographic or MRI changes.

The present findings have practical implications for clinicians managing symptomatic knee OA. Intra-articular methylprednisolone appears to be a more potent option for short- to intermediate-term pain relief and functional improvement than ketorolac in this setting. However, given the potential risks of repeated steroid injections, ketorolac may represent a useful alternative for patients in whom corticosteroids are relatively contraindicated (e.g. those at high risk for steroid-induced hyperglycaemia or infection) or for those requiring analgesia closer to planned surgery, where steroid use may be discouraged. [24–26,30] Shared decision-making should incorporate patient comorbidities, preferences, prior response to therapy and surgical plans.

This study has several limitations. First, the follow-up period of 12 weeks is relatively short and does not permit assessment of longer-term efficacy or structural outcomes for either intervention. Second, functional outcomes (OKS) are subjective

and may be influenced by psychosocial factors, coexisting conditions and adherence to physiotherapy, which were not controlled in detail. Third, the trial was conducted at a single tertiary centre, potentially limiting generalizability to other populations and practice settings. Fourth, the treating surgeon was not blinded to treatment allocation, which could theoretically introduce performance bias, although outcome measures were patient-reported. Finally, the study did not stratify results by radiographic severity (e.g. Kellgren–Lawrence grade), which may influence the magnitude of response to intra-articular therapy. [13,24–27]

Despite these limitations, the study adds to the limited body of evidence comparing IA ketorolac with corticosteroids in knee OA and is, to our knowledge, the first to directly compare single-dose methylprednisolone acetate with ketorolac without HA co-administration. Future research should explore optimal dosing regimens, the role of repeated injections, combinations with HA or other biologics, and longer-term structural and clinical outcomes, ideally in multicentre, blinded randomized controlled trials with imaging endpoints. [22–27]

In conclusion, both intra-articular ketorolac and methylprednisolone acetate significantly reduced pain and improved function in patients with knee OA; however, methylprednisolone produced superior improvements in VAS and OKS at 4 and 12 weeks. Given that both agents were well tolerated, clinicians may consider intra-articular corticosteroid as the preferred option for short-term symptom control, while recognizing ketorolac as a reasonable alternative when steroid use is limited or undesirable.

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