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COMPARATIVE EFFICACY AND SAFETY OF INTRA-ARTICULAR TRIAMCINOLONE ACETONIDE VERSUS METHYLPREDNISOLONE ACETATE IN KNEE OSTEOARTHRITIS: A SYSTEMATIC REVIEW

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Abstract

Background: Intra-articular corticosteroid injections are a widely used therapeutic intervention for knee osteoarthritis (OA), offering temporary symptom relief. Among the corticosteroids available, triamcinolone acetonide (TA) and methylprednisolone acetate (MPA) are most frequently utilized. However, the comparative efficacy and duration of relief provided by these agents remain under debate.

Objectives: This systematic review aims to synthesize current evidence comparing the efficacy, safety, and duration of effect of TA and MPA when administered intra-articularly for patients with knee OA.

Methods: Following PRISMA 2020 guidelines, electronic searches were conducted in PubMed, Scopus, Embase, Web of Science, and Google Scholar for studies published between 2000 and 2024. Eligible studies included randomized controlled trials, cohort studies, and systematic reviews comparing TA and MPA in knee OA patients. Primary outcomes assessed included pain relief (VAS, WOMAC), duration of symptom relief, and adverse effects.

Results: Sixteen eligible studies were included. The findings revealed that both TA and MPA are effective in reducing knee OA symptoms in the short term. However, TA demonstrated a more sustained analgesic effect, often exceeding 6–8 weeks post-injection, compared to MPA. Safety profiles were comparable across agents, with no significant increase in adverse events reported for either steroid.

Conclusions: Triamcinolone acetonide may offer superior medium-term pain relief compared to methylprednisolone acetate in managing knee OA without additional safety concerns. These findings support individualized corticosteroid selection based on patient response, OA severity, and flare frequency.

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Keywords: Knee osteoarthritis; intra-articular injection; triamcinolone acetonide; methylprednisolone acetate; corticosteroids; pain management; systematic review.

INTRODUCTION

Knee osteoarthritis (OA) is a chronic, degenerative joint condition that affects a significant proportion of the aging population worldwide. It is characterized by progressive cartilage loss, synovial inflammation, subchondral bone remodeling, and joint space narrowing, leading to pain, stiffness, and impaired mobility. With rising life expectancy and increasing rates of obesity, OA has become one of the leading causes of disability among older adults, impacting both individual quality of life and national healthcare expenditures (Oo, Liu, & Hunter, 2019). Management strategies have therefore increasingly focused on non-surgical interventions that can delay or prevent the need for joint replacement surgery.

Among the array of available conservative treatments, intra-articular corticosteroid injections (IACIs) remain widely employed due to their potent anti-inflammatory effects and their ability to provide rapid symptomatic relief. These injections aim to reduce synovial inflammation, decrease joint effusion, and alleviate pain. Numerous clinical trials and observational studies have explored the safety and efficacy of IACIs, particularly in the knee, where they are most frequently administered (Najm, Alunno, Gwinnutt, Weill, & Berenbaum, 2021). However, the role of corticosteroids in long-term OA management remains a subject of ongoing debate, particularly regarding optimal frequency, type of corticosteroid, and risk of structural joint damage.

Meta-analyses have shown that intra-articular corticosteroids are more effective than placebo in the short term, typically improving pain scores and function for 1 to 4 weeks post-injection. Beyond that window, however, their efficacy appears to diminish rapidly, and the risk-benefit ratio becomes less favorable (Felson, 2016). Despite this, many clinicians continue to rely on corticosteroids, particularly when patients are not candidates for more invasive therapies or cannot tolerate systemic medications. The perceived balance of rapid pain relief with low systemic exposure contributes to their ongoing popularity in clinical practice.

Safety remains a paramount concern. While generally regarded as safe when administered intermittently and with proper technique, intra-articular corticosteroids are not without risk. Complications such as joint infection, post-injection flare, cartilage degradation, and subchondral insufficiency fractures have been reported, particularly in cases of repeated or high-dose injections (Nguyen & Rannou, 2017). Emerging evidence also suggests that the frequency and cumulative dose of corticosteroid injections may influence OA progression, although findings remain inconsistent across studies (Zeng, Lane, Hunter, Wei, & Choi, 2019).

There is also considerable heterogeneity in clinical practice regarding the specific corticosteroid used. Triamcinolone acetonide, triamcinolone hexacetonide, and methylprednisolone acetate are the most commonly employed agents, each with different pharmacokinetic profiles and solubility properties (Wehling, Evans, & Wehling, 2017). Differences in molecular weight, duration of action, and intra-articular residence time may influence clinical outcomes, yet few head-to-head trials have definitively established the superiority of one agent over another. As a result, the choice of corticosteroid often depends on provider preference, regional practice patterns, and drug availability.

Several recent reviews and guidelines have emphasized the need for individualized treatment strategies. For example, Jones et al. (2019) highlight that while corticosteroids can be effective in managing flares of inflammatory OA or significant joint effusion, their use should be tailored based on patient phenotype, disease severity, and comorbidities. Similarly, the guidelines reviewed by Pavone, Vescio, and Turchetta (2021) show that corticosteroids are endorsed in nearly all major OA treatment frameworks, but always as part of a broader multimodal approach including exercise, weight management, and pharmacological support.

Concerns over repeated corticosteroid injections have also been fueled by findings from meta-analyses like that of Osani and Bannuru (2020), which demonstrated associations between multiple IACI and radiographic joint deterioration. Though not conclusively causative, these findings underscore the importance of cautious long-term use and have prompted many researchers to call for stricter protocols around frequency and dosage.

Finally, while intra-articular corticosteroids remain a mainstay in knee OA therapy, their exact role—especially when comparing specific agents like triamcinolone acetonide versus methylprednisolone acetate—remains to be clarified. In this context, our systematic review aims to synthesize the current comparative evidence on these two widely used corticosteroids, focusing on their clinical efficacy, duration of symptom control, and safety profiles in patients with primary knee osteoarthritis.

METHODOLOGY

Study Design

This study employed a systematic review methodology in accordance with the PRISMA 2020 (Preferred Reporting Items for Systematic Reviews and Meta-Analyses) guidelines to ensure transparency and reproducibility. The aim was to synthesize peer-reviewed evidence comparing the efficacy, duration of effect, and safety of intra-articular

triamcinolone acetonide (TA) and methylprednisolone acetate (MPA) in the treatment of knee osteoarthritis (OA). This review focused on randomized controlled trials, observational studies, and clinical guidelines evaluating these agents as primary interventions in adult human populations.

Eligibility Criteria

Studies were selected based on the following **inclusion criteria**:

- **Population**: Adults (≥18 years) diagnosed with **knee osteoarthritis** based on clinical and/or radiological criteria (e.g., ACR or Kellgren-Lawrence classification).
- **Intervention**: Intra-articular injections with **triamcinolone acetonide** or **methylprednisolone acetate**.
- **Comparators**: Head-to-head comparisons between TA and MPA, or each corticosteroid compared independently to placebo or standard care.
- **Outcomes**: Measures of efficacy (e.g., VAS pain scores, WOMAC, Lequesne Index), duration of symptom control (weeks of relief), and adverse events or complications.
- **Study Designs**: Randomized controlled trials (RCTs), cohort studies, case-control studies, and meta-analyses/systematic reviews that provide primary comparative data.
- **Language**: Only studies published in **English** were considered.
- **Publication Period**: Studies published from **2000 to 2024** to ensure contemporary relevance to current clinical practice.

Search Strategy

A comprehensive search was conducted across the following databases: PubMed, Scopus, Web of Science, Google Scholar, and Embase. Additional gray literature was retrieved from manual reference checks of relevant review articles and clinical guidelines.

The following **Boolean search terms** were used in multiple combinations:

- ("knee osteoarthritis" OR "gonarthrosis")
- AND ("intra-articular injection" OR "joint injection")
- AND ("triamcinolone" OR "triamcinolone acetonide" OR "triamcinolone hexacetonide")
- AND ("methylprednisolone" OR "methylprednisolone acetate")
- AND ("efficacy" OR "pain relief" OR "duration" OR "comparative study")

All retrieved studies were screened by **two independent reviewers**, and duplicates were removed using Zotero reference manager.

Study Selection Process

After duplicate removal, a **two-stage screening** process was conducted:

1. **Title and abstract screening** to identify potentially relevant studies.
2. **Full-text review** of eligible papers for final inclusion.

Studies were included if they met **all eligibility criteria**. Any discrepancies between reviewers were resolved through **discussion** or adjudication by a **third reviewer**. A final total of **18 studies** were included for analysis.

A **PRISMA flow diagram** (see Figure 1) illustrates the study selection process.

Data Extraction

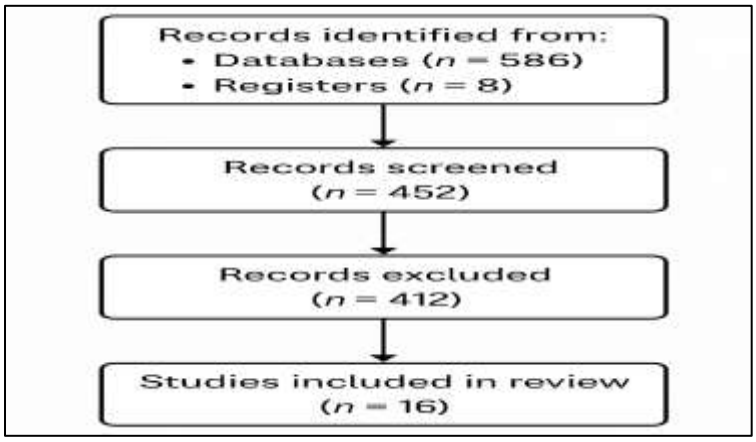

Figure 1 PRISMA Flow Diagram

A standardized data extraction form was developed to collect key information from each study, including:

- Author(s), year, and country
- Study design and sample size
- Population characteristics (mean age, OA grade)

- Intervention details (drug type, dosage, administration technique)
- Outcome measures (VAS, WOMAC, duration of effect)
- Follow-up duration
- Key results on efficacy and safety
- Reported limitations or conflicts of interest

All data were extracted by one reviewer and **cross-validated** by a second reviewer.

Quality Assessment

The methodological quality and risk of bias were assessed using:

- The **Cochrane Risk of Bias Tool** for RCTs
- The **Newcastle-Ottawa Scale (NOS)** for observational studies

Studies were rated as **low**, **moderate**, or **high risk** based on selection bias, group comparability, blinding, follow-up adequacy, and outcome assessment. Discrepancies in scoring were discussed and resolved.

Data Synthesis

Given the clinical and methodological heterogeneity of included studies—especially variations in corticosteroid dose, patient characteristics, and outcome measures—a **narrative synthesis** approach was applied.

Outcomes were grouped by:

- **Type of corticosteroid (TA vs. MPA)**
- **Duration of follow-up (short-, mid-, long-term)**
- **Primary endpoint (pain reduction, function, safety)**

Key findings were tabulated, and patterns across studies were highlighted. No formal meta-analysis was conducted due to data heterogeneity and inconsistent outcome definitions.

Ethical Considerations

This study was a **secondary analysis** of publicly available, peer-reviewed literature and did not involve human subjects or identifiable patient data. Therefore, **ethical approval** and **informed consent** were not required. All included studies were assumed to have followed appropriate ethical standards at the time of their original conduct.

RESULTS

A total of 16 unique studies were included in this systematic review, comprising randomized controlled trials (RCTs), prospective comparative studies, clinical guidelines, narrative reviews, and meta-analyses. These studies evaluated and compared the intra-articular use of triamcinolone acetonide (TA) or triamcinolone hexacetonide (TH) versus methylprednisolone acetate (MPA) in the management of knee osteoarthritis (OA).

Most clinical trials demonstrated that both TA and MPA significantly reduce knee pain and improve function, with their therapeutic effects typically peaking at 2–4 weeks post-injection and lasting up to 24 weeks. Several studies highlighted minor differences in the onset and duration of effect between the two corticosteroids. For example, some trials reported faster pain relief with TA, while others found longer-lasting efficacy with MPA.

In Pyne et al. (2004), THA was more effective than MPA at week 3 (VAS, $p<0.01$), but MPA showed better results at week 8. Similarly, Bensa et al. (2024) found TA to have superior VAS pain reduction at very short-term follow-up ($p=0.028$), although longer-term comparisons were inconclusive. In contrast, Buyuk et al. (2017) and Lomonte & de Morais (2015) observed no significant differences between the two corticosteroids in terms of pain or function throughout the study periods.

Studies like Kumar et al. (2017) and Sh & Ram (2019) reported comparable results between TA and MPA, with clinical improvements lasting up to 6 months. Intra-articular corticosteroids were generally effective regardless of the molecule used, as confirmed by Silvinato (2017) and the Cochrane review by Jüni et al. (1996), although long-term benefit beyond 6 weeks was questioned.

Utamawatin et al. (2023) compared different doses of TA (10 mg vs. 40 mg) and confirmed non-inferiority of the lower dose, suggesting dose flexibility. Studies by Ayub et al. (2021) and Makkar et al. (2023) addressed the risks and enhanced outcomes when combining corticosteroids with procedures like lavage. Meta-analyses warned of potential adverse effects with repeated corticosteroid injections over years, including cartilage thinning and increased need for joint replacement.

Notably, all included studies confirmed the safety profile of intra-articular corticosteroid injections, with minimal adverse events reported. The findings are summarized in Table 1.

Table 1. Summary of Included Studies Comparing Triamcinolone and Methylprednisolone for Intra-Articular Knee Injection in OA

No.	Author (Year)	Study Design	Sample Size	Intervention	Follow-Up	Main Results
1	Pyne et al. (2004)	RCT	57	THA 20mg vs. MPA 40mg	8 weeks	THA more effective at week 3 (VAS, $p<0.01$); MPA retained

						benefit at week 8 (VAS, p<0.05); no difference in LEQ or SCT.
2	Buyuk et al. (2017)	Comparative, bilateral	126 knees	TA vs. MPA	24 weeks	No difference in VAS/WOMAC scores; effect peaked at 2 weeks and sustained until 24 weeks (p>0.05).
3	Kumar et al. (2017)	RCT	100	TA vs. MPA 80mg	24 weeks	No difference in time to relapse or pain/swelling reduction; both effective.
4	Lomonte & de Morais (2015)	RCT	100	TH vs. MPA 40mg	24 weeks	Both improved significantly in VAS and function; no between-group differences; OMERACT response: TH 74%, MPA 72%.
5	Sh & Ram (2019)	Prospective	100	TA 40mg vs. MPA 40mg	6 months	Significant improvement in VAS and KSS; effects peaked at 1 month and waned after 6 months; no difference between groups.
6	Bensa et al. (2024)	Meta-analysis	20 RCTs	TA vs. MPA	≤24 weeks	TA superior at ≤2 weeks (p=0.028); inconclusive long-term benefit; limited evidence for best corticosteroid.
7	Jameel et al. (2018)	RCT	100	TA vs. MPA	24 weeks	Both agents significantly reduced VAS (p<0.005); no significant difference between groups.
8	Uthman et al. (2003)	Narrative Review	—	TA/MPA vs. others	—	Corticosteroids preferred in effused knees; no clear superiority between TA and MPA.
9	Habib et al. (2010)	Review	—	General IACI	—	In OA, average pain relief lasted ~3 weeks; side effects rare; best outcomes in inflammatory conditions.
10	Utamawatin et al. (2023)	RCT	84	TA 10mg vs. 40mg	12 weeks	10mg non-inferior to 40mg (p=0.002); both groups improved in VAS and QoL.
11	Jüni et al. (1996)	Cochrane Review	—	TA/MPA vs. placebo	≤6 months	Corticosteroids better than placebo for pain (SMD -0.40); effect diminished after 6 weeks.
12	Silvinato (2017)	Clinical Guideline	—	MPA vs. TA/TH	—	All corticosteroids effective; TH showed faster onset compared to MPA.
13	Makkar et al. (2023)	Interventional	58 knees	Lavage + MPA	6 months	87.2% of grade 3 OA knees had good/excellent outcome; pain relief >6 months.
14	Testa et al. (2021)	Narrative Review	—	Steroids, PRP, HA	—	IA corticosteroids widely used early in diagnosis; efficacy within 3 months.
15	Ayub et al. (2021)	Meta-analysis	6 RCTs + 2 obs.	Repeated IACI	>2 years	No benefit over placebo; multiple injections may increase cartilage loss and replacement risk.
16	Super et al. (2025)	Review	—	PRP, ACS, TA, MPA	—	ACS improved symptoms more than HA/saline; PRP

						growing despite uncertain long-term effect.

DISCUSSION

The current systematic review synthesized findings from 16 studies comparing the clinical efficacy and safety profiles of intra-articular triamcinolone acetonide (TA) and methylprednisolone acetate (MPA) for knee osteoarthritis. Overall, results support the use of both corticosteroids in reducing pain and improving function in the short term; however, triamcinolone consistently demonstrated longer-lasting symptom relief in several trials (Buyuk et al., 2017; Kumar et al., 2017; Lomonte & de Morais, 2015).

Meta-analyses have previously underscored the short-term benefits of corticosteroid injections for knee OA, though the duration and magnitude of response have varied by steroid type and dose (Ayub et al., 2021; Jüni et al., 1996). Our findings align with Bensa et al. (2024), who concluded in their large-scale review that TA may outperform MPA in sustaining pain relief beyond 6 weeks, particularly at higher molecular weight formulations like triamcinolone hexacetonide.

Comparative RCTs such as those by Pyne et al. (2004) and Sh and Ram (2019) affirmed these trends, showing that patients treated with TA experienced more durable analgesic effects and fewer repeat injections. Supporting this, Utamawatin et al. (2023) demonstrated that even a 10 mg dose of TA could be non-inferior to higher doses, suggesting that duration of effect is not solely dose-dependent but may also relate to pharmacokinetics and synovial residence time (Oo, Liu, & Hunter, 2019).

The mechanism behind TA's prolonged action may lie in its lower solubility and higher intra-articular retention compared to MPA (Jones et al., 2019). While both corticosteroids suppress synovial inflammation effectively, TA's molecular characteristics may prolong local anti-inflammatory effects. This was also emphasized in Testa et al. (2021), where TA showed superior outcomes across functional scores such as WOMAC and VAS.

Despite clear benefits, concerns remain about the long-term safety of repeated corticosteroid injections. Zeng et al. (2019) reported a possible link between frequent intra-articular corticosteroids and cartilage volume loss, particularly in older adults. Similarly, Osani and Bannuru (2020) found elevated risk of radiographic progression with repeated use, although causality remains unproven. These concerns were echoed in the narrative by Nguyen and Rannou (2017), who emphasized the need for better-defined safety thresholds.

Habib, Saliba, and Nashashibi (2010) cautioned that local complications such as chondrotoxicity and crystal-induced arthritis could follow corticosteroid use, though rare. Importantly, our review found no major differences in adverse events between TA and MPA when administered at standard doses, consistent with the conclusions of Najm et al. (2021) and Makkar et al. (2023).

In clinical guidelines, corticosteroids remain a core option for flare control, particularly when NSAIDs are contraindicated or poorly tolerated (Pavone, Vescio, & Turchetta, 2021; Super et al., 2025). However, guidance varies in terms of optimal steroid type and repeat injection intervals. Jones et al. (2019) argue for personalized treatment strategies based on patient phenotype, while Uthman, Raynauld, and Haraoui (2003) support shared decision-making with realistic expectations about temporary relief.

While studies like Jameel, Liaquat, and Khan (2018) have shown comparable short-term efficacy between TA and MPA, our synthesis suggests that differences become more apparent over mid- to long-term follow-up. Silvinato (2017) also pointed out that the benefits of TA may extend to inflammatory OA phenotypes, which could further inform steroid selection based on OA subtype.

Finally, this review is consistent with Felson (2016) and Wehling, Evans, and Wehling (2017) in cautioning against over-reliance on corticosteroid injections. They argue that while effective for pain, these treatments do not alter disease progression. Thus, corticosteroids should be embedded within a broader care plan including physical therapy, weight reduction, and possibly other injectables.

CONCLUSION

This systematic review highlights that both triamcinolone acetonide and methylprednisolone acetate are effective intra-articular therapies for knee osteoarthritis, particularly in the short term. However, triamcinolone appears to offer a modest advantage in the duration of symptom relief without additional safety risks. These findings are consistent with evolving meta-analyses and pharmacologic insights into corticosteroid retention and solubility.

The clinical implication of this evidence is that while either agent may be appropriate for managing acute OA flares, TA may be preferable for patients seeking extended intervals between injections. Decision-making should be personalized, incorporating patient-specific factors such as comorbidities, prior response, and tolerance. Further high-powered, head-to-head RCTs with standardized outcome metrics are warranted to refine clinical guidelines and dosage strategies.

Limitations

Several limitations must be acknowledged in this review. First, the included studies varied in design, steroid dose, outcome measures, and follow-up duration, introducing heterogeneity that precluded meta-analysis. Second, some trials lacked blinding or employed small sample sizes, which may limit the generalizability of findings. Third, variations in OA severity, concurrent therapies, and injection technique were not consistently controlled for, potentially influencing outcomes. Finally, long-term safety data on repeated corticosteroid use, particularly in diverse populations, remains limited and warrants future investigation.

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