

A COMPARATIVE EVALUATION OF INTRA-ARTICULAR TRIAMCINOLONE ACETONIDE VERSUS METHYLPREDNISOLONE ACETATE FOR KNEE OSTEOARTHRITIS

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Abstract

Background: Knee osteoarthritis (KOA) is a leading cause of pain and disability worldwide. Intra-articular corticosteroids, including triamcinolone acetonide (TAC) and methylprednisolone acetate (MPA), are widely used for short-term symptomatic relief, but their comparative effectiveness remains unclear.

Objective: To comparatively evaluate the clinical efficacy, pain reduction, functional improvement, and short-term safety of intra-articular TAC versus MPA in patients with symptomatic knee osteoarthritis.

Methods: A comparative cross-sectional study was conducted over four months at two clinical centers in Khyber Pakhtunkhwa, Pakistan. A total of 126 adults aged 40–75 years with clinically and radiologically confirmed KOA (Kellgren–Lawrence Grades I–III) were enrolled and allocated to receive either intra-articular TAC (n=63) or MPA (n=63). Pain was assessed using the Visual Analog Scale (VAS), and function was evaluated using a six-item WOMAC/function score. Assessments were performed at baseline and at a single post-injection follow-up. Between-group differences were analyzed using Mann–Whitney U tests and multiple linear regression to adjust for baseline imbalances.

Results: Both treatment groups demonstrated significant improvement in pain and function. However, MPA was associated with significantly greater VAS improvement (mean 4.508 vs 1.937; $U=178.000$, $Z=-8.960$, $p<0.001$; $r\approx 0.80$) and greater improvement in the six-item WOMAC/function score (mean 10.206 vs 5.984; $U=215.000$, $Z=-8.688$, $p<0.001$; $r\approx 0.77$). Patient satisfaction, willingness to recommend treatment, and quality-of-life improvement were also significantly higher in the MPA group (all $p<0.001$). Local adverse events were infrequent and similar between groups; systemic effects (headache) were reported only in

the TAC group ($p=0.012$).

Conclusion: Intra-articular MPA provides superior short-term pain relief and functional improvement compared with TAC in patients with mild-to-moderate knee osteoarthritis. Both injections appear safe in the short term. These findings support the use of MPA when rapid symptomatic control is the primary treatment goal, although longer-term randomized trials are needed to confirm durability and safety.

Introduction

Knee osteoarthritis (KOA) is a chronic joint disorder characterised by pain, stiffness, and progressive limitations in physical function. Although cartilage degeneration is a prominent feature, the disease involves the entire joint, including subchondral bone, synovium, menisci, ligaments, and surrounding muscles. Interactions between mechanical loading, inflammatory activity, and metabolic changes contribute to its heterogeneous clinical presentation. Patients may experience difficulty walking, climbing stairs, and performing routine activities, with consequences for independence and quality of life. This complexity makes effective management challenging and highlights the importance of treatments that provide meaningful symptomatic improvement within a broader programme of conservative care. (1)

The growing epidemiological burden of KOA strengthens the need to evaluate accessible treatments. Using Global Burden of Disease 2021 estimates, Ouyang and Dai reported approximately 374.7 million prevalent cases worldwide, with increasing disease burden between 1990 and 2021. Their analysis identified higher prevalence and incidence among women and projected further increases in case numbers through 2045. Population growth and ageing contribute to the expanding demand for care. These findings establish KOA as a substantial public health concern and support research directed towards reducing disability, improving symptom control, and informing treatment selection in populations served by different healthcare systems. (2)

Inflammation provides a biological rationale for corticosteroid treatment, but its contribution to symptoms requires careful interpretation. In a

longitudinal magnetic resonance imaging study, Hill et al. found that changes in synovitis were associated with changes in knee pain, although the relationship was modest. Changes in synovitis were not associated with cartilage loss in that investigation. The findings suggest that synovial inflammation is a relevant therapeutic target while also demonstrating that pain and structural deterioration are not interchangeable outcomes. Consequently, improvement following an anti-inflammatory intervention should be evaluated as symptomatic benefit without assuming that the intervention prevents cartilage degeneration or modifies disease progression. (3)

Management therefore requires an individualised approach addressing symptoms, physical capacity, and modifiable contributors to disability. The updated European Alliance of Associations for Rheumatology recommendations emphasise education, self-management, appropriately prescribed exercise, and support for maintaining a healthy weight or achieving weight loss. Footwear, walking aids, assistive devices, and behavioural strategies may also form part of care according to individual needs. These recommendations position non-pharmacological interventions as core management rather than optional additions. Within this framework, an injection should be assessed according to its contribution to the patient's overall treatment goals, including whether symptom relief supports participation in everyday activities and rehabilitation. (4)

Evidence comparing treatment strategies reinforces the need to preserve this broader perspective. Deyle et al. randomly assigned 156 patients with knee osteoarthritis to physical therapy or intra-articular glucocorticoid injection. At one year, patients receiving physical therapy had less pain and functional disability, measured

using the Western Ontario and McMaster Universities Osteoarthritis Index (WOMAC), than those receiving injections. This finding does not resolve which corticosteroid formulation offers better early relief, but it shows that the preferred approach can depend on the outcome and time horizon. Comparative injection research should therefore complement longer-term conservative management rather than displace established rehabilitation strategies. (5)

Intra-articular corticosteroids remain relevant because clinical trials have demonstrated improvements in pain and function after treatment. Triamcinolone acetonide (TAC) and methylprednisolone acetate (MPA) are among the agents evaluated for symptomatic knee disease. Their shared therapeutic purpose does not establish equivalent effectiveness, and a useful comparison must consider the specific preparation, dose, patient population, and assessment schedule. Moreover, improvement within a treatment group cannot alone determine whether that agent is superior to another. Direct comparisons are needed to separate the question of whether patients improve after an injection from the more clinically specific question of which injection produces better outcomes. (6,7)

Direct evidence favouring MPA at early assessments was reported by Yavuz et al. in a prospective randomised study of 120 patients with painful KOA. Participants received methylprednisolone acetate, triamcinolone acetonide, betamethasone disodium phosphate, or saline, with 30 patients in each group. Pain and function were assessed before treatment and at the first, third, sixth, and twelfth weeks. The investigators reported that MPA produced greater analgesic benefit than the other agents through the sixth week. This study provides a relevant basis for comparing MPA with TAC, while its limited group sizes and scheduled assessment intervals should be considered when interpreting the apparent advantage. (6)

Other comparative findings are less supportive of a consistent difference between corticosteroid preparations. Lomonte et al. conducted a randomised, double-blinded study involving 100

patients with symptomatic KOA and Kellgren-Lawrence grade II or III disease. Participants received either 40 mg triamcinolone hexacetonide or 40 mg methylprednisolone acetate. Both groups improved in pain and functional outcomes, without significant between-group differences, and improvements were maintained during the 24-week study. However, triamcinolone hexacetonide is a different formulation from triamcinolone acetonide. The findings are therefore informative about corticosteroid selection but should not be presented as direct evidence that TAC and MPA have equivalent effects. (7)

Evidence from other arthritic conditions also requires attention to clinical applicability. Kumar et al. directly compared MPA and TAC in a randomised trial involving patients with chronic inflammatory arthritis and reported no significant difference in time to relapse. Although the agents match those of interest in KOA, the underlying disease population differs. Results obtained in inflammatory arthritis cannot automatically establish comparative effectiveness in osteoarthritis. Taken together with the KOA studies, this evidence illustrates why differences in diagnosis and formulation must be retained when reviewing corticosteroid research, rather than combining all knee injection studies into a single conclusion about superiority. (8)

The choice of outcome is equally important when evaluating treatment response. Pain intensity and physical function describe related but distinct aspects of the patient's experience. An injection may reduce discomfort without producing a corresponding improvement in activities requiring strength, balance, or sustained loading. Studies using both pain measures and functional indices consequently provide a more informative assessment than those relying on pain alone. Patient satisfaction and perceived improvement in daily life can add complementary information, although these outcomes should be distinguished from objective performance. Clear identification of the questionnaire and scoring method is essential for interpreting changes and comparing findings across studies. (5,7)

Safety further complicates the interpretation of symptomatic benefit. McAlindon et al. randomised 140 patients with symptomatic KOA to receive 40 mg intra-articular triamcinolone acetonide or saline every three months for two years. Repeated triamcinolone treatment resulted in greater cartilage loss without a significant advantage in pain at the scheduled assessments. These findings raise concerns about that repeated-injection regimen, but they do not directly determine the relative safety of a single TAC injection compared with MPA. They also demonstrate why short-term clinical improvement and long-term structural safety require separate evaluation, with conclusions limited to the dosing schedule and follow-up actually studied. (9)

Clinical heterogeneity also matters substantially when assessing the relevance of a comparison. Age, body weight, previous injury, and the extent of joint involvement can contribute to differences in the presentation of KOA. Patients with similar radiographic disease may nevertheless have different priorities, ranging from relief during walking to improved ability to manage household activities. A treatment evaluation should therefore describe whom it represents and avoid extending its conclusions to patients with substantially different clinical needs. In particular, findings in mild or moderate disease require cautious interpretation when considering advanced disease, where structural limitations and the potential need for surgery alter the clinical context. (1,2,4)

The available literature consequently provides a rationale for further comparison rather than a definitive hierarchy of corticosteroid agents. Early analgesic differences reported in some studies coexist with findings of similar outcomes in studies using another triamcinolone formulation or a different arthritis population. Variation in study design, outcome measurement, and follow-up further limits simple comparisons. A clinically useful evaluation should specify the exact corticosteroid administered and examine pain, function, and adverse events within the same population. The interpretation should also distinguish statistical differences from benefits that matter to patients, particularly when

treatment is intended to improve mobility and participation in daily activities. (6–9)

Locally generated evidence can contribute to this question by describing outcomes among patients attending the services in which these injections are used. In the present study, the relevant setting comprises two clinical centres in Khyber Pakhtunkhwa, Pakistan. Evaluating both treatments in this setting can inform the applicability of the wider comparative literature without assuming that findings from other populations will be reproduced. Such evidence remains most useful when the clinical characteristics of participants and the scope of assessment are clearly described. Differences in baseline symptoms must also be considered before an observed treatment association is interpreted as evidence of superiority. (6–8)

Accordingly, this study aimed to compare the short-term clinical outcomes of intra-articular TAC and MPA in adults with symptomatic, clinically and radiologically confirmed KOA of Kellgren–Lawrence grades I–III. The evaluation focused on pain reduction, change in the available six-item WOMAC/function score, patient-reported satisfaction and quality-of-life improvement, and recorded adverse events. By assessing both symptom burden and perceived benefit, the study sought to contribute evidence relevant to corticosteroid selection in the participating clinical services. Its focus on short-term outcomes addresses the immediate comparative treatment question, while the broader literature underscores the separate need to establish durability and structural safety. (6,7,9)

Methodology

A comparative clinical study was conducted over a period of four months at Dr. Naeem Shah Clinic and Dr. Arshad Iqbal Brain and Spine Clinic, Lower Timergara, Dir, Khyber Pakhtunkhwa, Pakistan, to compare the short-term clinical outcomes of intra-articular triamcinolone acetonide (TAC) and methylprednisolone acetate (MPA) in patients with symptomatic knee osteoarthritis (KOA). A total of 126 participants were included in the study, with 63 participants

receiving TAC and 63 receiving MPA. The required sample size was calculated using a 95% confidence level and 80% statistical power, assuming a pooled standard deviation of 2 and a minimum detectable difference of 1. Participants were recruited through non-probability convenience sampling.

Eligible participants were adults aged 40–75 years with clinically and radiologically confirmed KOA classified as Kellgren–Lawrence (KL) grades I–III. Participants were required to have persistent knee pain for at least three months, a baseline Visual Analogue Scale (VAS) score of ≥ 4 , and functional limitations affecting activities such as walking or stair climbing. Participants were also required to provide informed consent and demonstrate willingness to comply with the study procedures and follow-up assessment. Patients with KL grade IV osteoarthritis or those requiring immediate surgical intervention or arthroplasty were excluded. Other exclusion criteria included previous knee surgery or major ligament reconstruction, inflammatory, infectious, or crystal-induced arthritis, uncontrolled diabetes, severe cardiovascular disease, hematological disorders, pregnancy or lactation, and known hypersensitivity to corticosteroids or injection materials. Participants who had received an intra-articular injection in the affected knee within the preceding three months were also excluded.

Following eligibility assessment and baseline data collection, participants were categorized into two treatment groups according to the corticosteroid administered. The TAC group received an intra-articular triamcinolone acetonide injection, whereas the MPA group received an intra-articular methylprednisolone acetate injection. The injection procedure was performed under aseptic precautions. The study questionnaire recorded the administered corticosteroid and dose, together with procedure-related and post-injection outcomes. The available dose categories documented in the study instrument were 40, 80, and 120 mg. Baseline information included demographic characteristics, clinical characteristics, radiographic KL grade, pain severity, and functional status. Pain severity was

assessed using the Visual Analogue Scale (VAS), including pain at rest and during activities such as walking and stair climbing. Functional status was assessed using six available items derived from the WOMAC framework, addressing activities including rising from a chair, walking on a flat surface, climbing stairs, squatting or kneeling, morning stiffness, and limitations in daily activities.

Clinical outcomes were assessed by comparing pre-injection and post-injection measurements. The primary outcomes were changes in pain intensity and knee-related functional status, represented by the VAS composite score and the available six-item WOMAC/function score, respectively. Secondary outcomes included patient satisfaction, willingness to recommend the treatment, perceived improvement in quality of life, and treatment-related adverse events. The adverse-event assessment included immediate post-injection discomfort, post-injection flare, local skin changes, systemic effects such as headache, flushing or palpitations, and emergency visits related to the injection. Although the original data-collection protocol described assessments at two and four weeks following injection, the final analyzed dataset contained one available post-injection assessment. Therefore, the present analysis focused on the documented short-term change from baseline to the available post-injection assessment and did not evaluate treatment duration or time to recurrence of pain. The study was conducted in accordance with the ethical principles of the Institutional Review Board. Written informed consent was obtained from all participants after they were informed about the study objectives, procedures, potential risks, and their right to withdraw from the study without consequences. Personally identifiable information was not recorded, and the collected data were securely maintained and used exclusively for research purposes.

Statistical analysis was performed using IBM SPSS Statistics version 27. Continuous variables were summarized using means and standard deviations, while categorical variables were presented as frequencies and percentages. Baseline

characteristics and clinical outcomes were summarized for both treatment groups. Between-group differences in treatment-related improvement were assessed using appropriate statistical tests, including the Mann-Whitney U test where the assumptions for parametric analysis were not met. Pre- and post-injection changes in the available six-item WOMAC/function score were also evaluated. Multiple linear regression analyses were performed to examine the association between treatment group and post-injection pain and functional outcomes while adjusting for baseline outcome measures.

Categorical outcomes, including patient satisfaction and adverse events, were compared between treatment groups using the chi-square test where appropriate. A two-sided p-value of <0.05 was considered statistically significant.

Results

4.1 Participant Demographic and Clinical Characteristics

A total of 126 patients with knee osteoarthritis were included. The treatment groups were balanced in size, with 63 patients receiving MPA and 63 receiving TAC.

Table:0:1 Overall demographic and clinical characteristics of participants (N=126)

Characteristic	Category	n	%
Treatment	Methylprednisolone acetate	63	50.0
	Triamcinolone acetonide	63	50.0
Age group	40–49 years	26	20.6
	50–59 years	48	38.1
	60–69 years	32	25.4
	70 years or above	20	15.9
Gender	Male	40	31.7
	Female	86	68.3
Lifestyle	Sedentary	83	65.9
	Light work	40	31.7
	Moderate work	3	2.4
BMI category	Underweight	3	2.4
	Normal	47	37.3
	Overweight	66	52.4
	Obese	10	7.9
Affected knee	Right	62	49.2
	Left	17	13.5
	Bilateral	47	37.3
Kellgren–Lawrence grade	Grade I	59	46.8
	Grade II	43	34.1
	Grade III	24	19.0
Duration of knee symptoms	6 months–2 years	18	14.3
	2–5 years	50	39.7
	>5 years	58	46.0
Comorbidity	None	72	57.1
	Diabetes	29	23.0
	Hypertension	23	18.3
	Heart disease	1	0.8
	Thyroid disorder	1	0.8

The sample was mostly female (68.3%), with many participants in their 50–59-year bent (38.1%). 65.9% were sedentary and 52.4% were overweight. In addition, the analysed cohort was predominantly affected in the right knee – 49.2% – bilateral involvement was present in 37.3% of cases. By radiographic discrimination, Grade I

disease was the most common (46.8%) followed by Grade II (34.1%) and Grade III (19.0%). Almost half (46.0%) of participants had symptoms for longer than five years. Comorbidities Diabetes and hypertension were the most commonly documented comorbidities.

4.2 Baseline Comparability of the Treatment Groups

Table:0:2: Baseline categorical comparison between MPA and TAC groups

Variable	Pearson χ^2	df	p-value	Conclusion
Age group	2.187	3	0.534	No significant difference
Gender	21.098	1	<0.001	Significant difference
BMI category	4.682	3	0.197	No significant difference
Kellgren–Lawrence grade	3.300	2	0.192	No significant difference
Duration of symptoms	0.611	2	0.737	No significant difference
Comorbidity	6.225	4	0.183	No significant difference

No baseline characteristics showed statistically significant differences between the treatment groups (all $p>0.05$), indicating broad comparability across the groups with respect to age, BMI category, Kellgren–Lawrence grade, duration of symptoms and comorbidity status.

The distribution of females, however, differed between groups ($\chi^2=21.098$, $df=1$, $p<0.001$), with 87.3% of females in the MPA group versus 49.2% in the TAC group. Unadjusted comparisons of treatment effects should therefore be interpreted in light of this baseline imbalance.

4.3 Distribution of Demographic Variables by Treatment Group

Table:0:3: Table Distribution of key baseline characteristics by treatment group

Characteristic	MPA (n=63)	TAC (n=63)
Age 40–49	12 (19.0%)	14 (22.2%)
Age 50–59	28 (44.4%)	20 (31.7%)
Age 60–69	14 (22.2%)	18 (28.6%)
Age ≥ 70	9 (14.3%)	11 (17.5%)
Male	8 (12.7%)	32 (50.8%)
Female	55 (87.3%)	31 (49.2%)
Underweight	3 (4.8%)	0 (0.0%)
Normal BMI	23 (36.5%)	24 (38.1%)
Overweight	34 (54.0%)	32 (50.8%)
Obese	3 (4.8%)	7 (11.1%)
KL Grade I	27 (42.9%)	32 (50.8%)
KL Grade II	20 (31.7%)	23 (36.5%)
KL Grade III	16 (25.4%)	8 (12.7%)
Symptoms 6 months–2 years	10 (15.9%)	8 (12.7%)
Symptoms 2–5 years	23 (36.5%)	27 (42.9%)
Symptoms >5 years	30 (47.6%)	28 (44.4%)
No comorbidity	31 (49.2%)	41 (65.1%)
Diabetes	19 (30.2%)	10 (15.9%)

Hypertension	12 (19.0%)	11 (17.5%)
Heart disease	0 (0.0%)	1 (1.6%)
Thyroid disorder	1 (1.6%)	0 (0.0%)

The two groups had similar distributions across age, BMI, radiographic grade, symptom duration and comorbidity categories. The most pronounced difference was gender distribution, as reflected by the significant chi-square result in Table 4.2.

Although Grade III disease was numerically more common in the MPA group (25.4%) than the TAC group (12.7%), the overall difference in Kellgren–Lawrence grade was not statistically significant.

4.4 Baseline Pain and Functional Scores

Table 0:4: Baseline comparison of pain and functional scores

Outcome	MPA	TAC	Test	p-value
Pre-injection VAS composite	5.0317 ± 0.6949	3.7619 ± 0.8929	Welch t=8.908, df=116.946	<0.001
Pre-injection six-item WOMAC/function score	12.2857 ± 1.8177	11.6032 ± 2.4727	Welch t=1.765, df=113.864	0.080

Baseline VAS severity was significantly higher in the MPA group than in the TAC group (mean difference=1.270, p<0.001), indicating clinically relevant baseline imbalance in pain severity. In contrast, the baseline six-item WOMAC/function

score did not differ significantly between groups (p=0.080). Because baseline VAS differed significantly, interpretation of the unadjusted change in VAS should be made alongside the adjusted regression analysis.

4.5 Pre- and Post-injection Pain Severity

Table 0:5: Distribution of VAS pain categories before and after injection

Assessment	No pain	Mild	Moderate
Pain at rest – pre	20 (15.9%)	85 (67.5%)	21 (16.7%)
Pain at rest – post	122 (96.8%)	4 (3.2%)	0 (0.0%)
Pain during walking – pre	3 (2.4%)	49 (38.9%)	74 (58.7%)
Pain during walking – post	93 (73.8%)	33 (26.2%)	0 (0.0%)
Pain during stair climbing – pre	0 (0.0%)	22 (17.5%)	104 (82.5%)
Pain during stair climbing – post	33 (26.2%)	75 (59.5%)	18 (14.3%)

Figure 1: Pain Severity Distribution (%)

Pain was more pronounced during activity compared to rest, in particular during stair ascent with 82.5% reporting moderate pain. Compared to before injection, the distribution significantly shifted towards lower pain categories. At rest, 96.8% reported no pain post-injection compared

with 15.9% pre-injection; during walking, the proportion in the no-pain category increased from 2.4% to 73.8% Although fewer often reported residual symptoms during this more high-Demand activity, stair-climbing pain too improved.

Table 0:6: Descriptive statistics for primary pain and functional outcomes

Outcome	MPA (n=63)	TAC (n=63)
VAS composite – pre	5.032 ± 0.695; median 5; IQR 0	3.762 ± 0.893; median 4; IQR 1
VAS composite – post	0.524 ± 0.618; median 0; IQR 1	1.825 ± 0.814; median 2; IQR 1
VAS improvement	4.508 ± 1.045; median 5; IQR 1	1.937 ± 1.030; median 2; IQR 2
Six-item WOMAC/function – pre	12.286 ± 1.818; median 12; IQR 2	11.603 ± 2.473; median 12; IQR 4
Six-item WOMAC/function – post	2.079 ± 1.473; median 2; IQR 2	5.619 ± 1.930; median 5; IQR 3
WOMAC/function improvement	10.206 ± 2.164; median 10; IQR 3	5.984 ± 1.690; median 6; IQR 2

Both treatments were associated with improvement in pain and function, but the magnitude of improvement was consistently greater in the MPA group. Mean VAS improvement was 4.508 in the MPA group compared with 1.937 in the TAC group. Similarly,

mean six-item WOMAC/function improvement was 10.206 versus 5.984, respectively. The corresponding medians also demonstrate the same pattern, with median VAS improvement of 5 versus 2 and median WOMAC/function improvement of 10 versus 6.

4.7 Internal Consistency of the Six-item Questionnaire

Table 0:7: Reliability analysis of the available six questionnaire items

Scale	Cronbach's α	Items	Complete cases
Pre-injection six-item function/stiffness score	0.916	6	11 complete cases
Post-injection six-item function/stiffness score	0.695	6	101 complete cases

The six available pre-injection items demonstrated high internal consistency (Cronbach's $\alpha=0.916$), whereas the post-injection scale showed acceptable internal consistency ($\alpha=0.695$). However, the pre-injection alpha was based on only 11 complete cases because of listwise deletion. These reliability

estimates therefore provide supportive rather than definitive evidence of measurement consistency. Most importantly, these results apply only to the six items available in the dataset and should not be interpreted as reliability estimates for the full 24-item WOMAC instrument.

4.8 Assessment of Normality of Change Scores

Table 0:8: Normality assessment of primary change scores

Change score	Normality result	Decision	Primary inferential test
VAS improvement	Shapiro-Wilk significant; $p<0.001$	Non-normal	Mann-Whitney U
WOMAC/function improvement	Shapiro-Wilk significant; $p=0.003$	Non-normal	Mann-Whitney U

The change scores did not satisfy the normality assumption. Therefore, the Mann–Whitney U test was selected as the primary between-group

comparison rather than relying on parametric comparisons of change scores.

4.9 Primary Between-group Efficacy Analysis

Table 0:9: Mann–Whitney U comparison of treatment-related improvement

Outcome	MPA mean rank	TAC mean rank	U	Z	p-value	Effect size r
VAS improvement	92.17	34.83	178.000	-8.960	<0.001	$r \approx 0.80$
WOMAC/function improvement	91.59	35.41	215.000	-8.688	<0.001	$r \approx 0.77$

There were statistically significant between-group differences in both primary outcomes. MPA produced significantly greater VAS improvement than TAC ($U=178.000$, $Z=-8.960$, $p<0.001$), with a very large rank-based effect ($r \approx 0.80$). Likewise, MPA produced significantly greater improvement in the six-item WOMAC/function score than TAC ($U=215.000$, $Z=-8.688$, $p<0.001$; $r \approx 0.77$). Thus, the primary inferential analysis strongly favors MPA for the observed post-injection pain and functional improvement.

4.10 Within-group Pre/Post Analysis

The supplied files contained several attempted paired analyses. The first paired-Wilcoxon syntax was invalid, and a later split-file Wilcoxon analysis produced insufficient valid cases for the VAS comparison. A paired-samples analysis of the six-item WOMAC/function score using all 126 cases was available and showed a significant overall pre/post reduction.

Table 0:10: Paired pre/post comparison for the available six-item WOMAC/function score

Outcome	Pre mean $\pm$ SD	Post mean $\pm$ SD	Mean reduction	t	df	p-value
Six-item WOMAC/function score	11.9444 $\pm$ 2.1884	3.8492 $\pm$ 2.4660	8.0952	31.673	125	<0.001

The six-item WOMAC/function score decreased significantly from baseline to post-injection assessment, with a mean reduction of 8.095 points ($t=31.673$, $df=125$, $p<0.001$). Because lower scores indicate less difficulty/less symptom burden in the

coded questionnaire, this result demonstrates substantial overall improvement after injection. The within-group result should be interpreted as an overall pre/post change and does not replace the primary between-treatment comparison.

4.11 Regression Analysis

Table 0:11: Multiple linear regression models for post-injection outcomes

Dependent outcome	R	R ²	Adj. R ²	Model test	p	Key coefficients
Post-injection six-item WOMAC/function score	0.806	0.650	0.644	$F(2,123)=114.274$	<0.001	Treatment $B=3.821$, $\beta=0.778$, $p<0.001$; baseline WOMAC $B=0.413$,

						$\beta=0.366$, $p<0.001$
Post-injection composite VAS	0.674	0.455	0.446	$F(2,123)=51.276$	<0.001	Treatment $B=1.387$, $\beta=0.716$, $p<0.001$; baseline VAS $B=0.067$, $\beta=0.071$, $p=0.410$

The adjusted WOMAC/function model explained 65.0% of the variance in the post-injection six-item score (adjusted $R^2=0.644$; $p<0.001$). Both baseline WOMAC score and treatment group were significant predictors. With treatment coded as MPA=1 and TAC=2, the positive treatment coefficient ($B=3.821$) indicates a substantially higher post-injection function score in the TAC group, consistent with less improvement compared with MPA. The adjusted

VAS model explained 45.5% of the variance (adjusted $R^2=0.446$; $p<0.001$). Treatment group remained a strong significant predictor ($B=1.387$, $\beta=0.716$, $p<0.001$), whereas baseline VAS was not a significant independent predictor after treatment was included ($p=0.410$). These adjusted analyses support the primary finding that MPA was associated with better post-injection pain and functional outcomes.

4.12 Patient Satisfaction, Recommendation and Quality of Life

Table 0:12: Patient satisfaction by treatment group

Satisfaction category	MPA (n=63)	TAC (n=63)	Total
Neutral	0 (0.0%)	20 (31.7%)	20 (15.9%)
Satisfied	18 (28.6%)	40 (63.5%)	58 (46.0%)
Very satisfied	45 (71.4%)	3 (4.8%)	48 (38.1%)

Satisfaction was substantially higher among MPA recipients. Very high satisfaction was reported by 71.4% of MPA recipients compared with only 4.8% of TAC recipients, while 31.7% of TAC

recipients remained neutral. The association between treatment group and satisfaction was statistically significant (Pearson $\chi^2=65.095$, $df=2$, $p<0.001$).

Table 0:13: Recommendation of treatment-by-treatment group

Recommendation	MPA (n=63)	TAC (n=63)	Total
Probably yes	17 (27.0%)	59 (93.7%)	76 (60.3%)
Definitely yes	46 (73.0%)	4 (6.3%)	50 (39.7%)

All participants indicated at least a probable willingness to recommend their treatment, but the strength of recommendation differed markedly between groups. A definite recommendation was

reported by 73.0% of MPA recipients compared with 6.3% of TAC recipients. This association was statistically significant (Pearson $\chi^2=58.491$, $df=1$, $p<0.001$).

Table 0:14: Patient-reported quality-of-life improvement by treatment group

QOL category	MPA (n=63)	TAC (n=63)	Total
No improvement	1 (1.6%)	16 (25.4%)	17 (13.5%)
Moderate improvement	13 (20.6%)	42 (66.7%)	55 (43.7%)
Significant improvement	49 (77.8%)	5 (7.9%)	54 (42.9%)

A significantly greater proportion of MPA recipients reported significant quality-of-life improvement (77.8%) compared with TAC recipients (7.9%). Conversely, no improvement was reported by 25.4% of TAC recipients versus

only 1.6% of MPA recipients. The association between treatment group and quality-of-life improvement was statistically significant (Pearson $\chi^2=64.378$, $df=2$, $p<0.001$).

4.13 Safety and Adverse Events

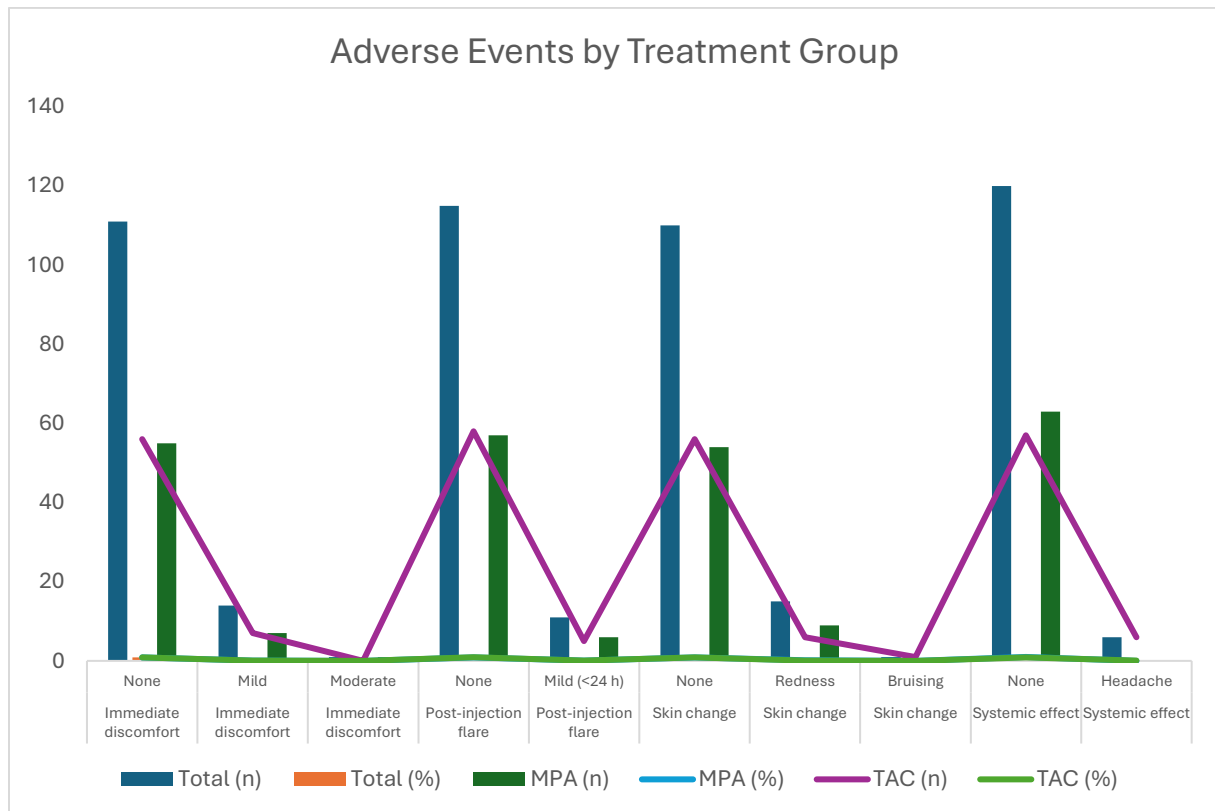


Figure 2: Adverse Events by Treatment Group

Most participants experienced no immediate discomfort (88.1%), no post-injection flare (91.3%), and no injection-site skin change (87.3%). Mild discomfort occurred in 11.1%, while moderate immediate discomfort was rare (0.8%). Mild post-injection flare was reported in

8.7%. Redness was the most frequent local skin change (11.9%), whereas bruising was uncommon (0.8%). No systemic effect was recorded in 95.2% of participants; headache occurred in 4.8% overall and was reported only in the TAC group.

Table 15: Statistical comparison of adverse events between treatment groups

Adverse event	Pearson χ^2	df	p-value
Immediate discomfort	1.009	2	0.604
Post-injection flare	0.100	1	0.752
Skin change	1.636	2	0.441
Systemic effect	6.300	1	0.012

There were no statistically significant differences between MPA and TAC groups for immediate discomfort, post-injection flare, or skin changes (all $p > 0.05$). However, systemic effects differed significantly between groups ($\chi^2 = 6.300$, $df = 1$, $p = 0.012$), reflecting the occurrence of headache in six TAC recipients and none in the MPA group. Because several low-frequency categories had small expected counts, the systemic-effect result should be interpreted with appropriate caution and, where required, confirmed using an exact test.

Discussion:

In this comparative study of 126 patients with symptomatic knee osteoarthritis, both methylprednisolone acetate (MPA) and triamcinolone acetonide (TAC) were associated with improvements in pain and function. However, MPA recipients demonstrated greater mean reductions in pain scores (4.508 versus 1.937) and the six-item WOMAC/function score (10.206 versus 5.984), with both comparisons reaching statistical significance ($p < 0.001$). These findings indicate an association between MPA administration and better outcomes at the recorded post-injection assessment, rather than establishing causal or sustained superiority.

The greater pain reduction associated with MPA is consistent with Yavuz et al., who reported greater early analgesic benefit with MPA than other corticosteroid preparations in knee osteoarthritis. Conversely, Lomonte et al. found no significant difference between MPA and triamcinolone hexacetonide. That comparison involved a different triamcinolone formulation and therefore cannot establish equivalence between MPA and TAC. These contrasting findings emphasise the importance of formulation, study population, and assessment timing when interpreting comparative corticosteroid effectiveness. (6,7)

Baseline differences require particular consideration. The MPA group had higher initial pain scores and a greater proportion of women than the TAC group. Higher baseline pain provides greater scope for improvement and may influence change scores. Although treatment remained associated with post-injection outcomes after adjustment for the corresponding baseline score, these models do not eliminate residual confounding, particularly from sex imbalance and other unmeasured characteristics. The observed differences should therefore be interpreted cautiously.

Functional improvements and patient-reported outcomes consistently favoured MPA. Very high satisfaction was reported by 71.4% of MPA recipients compared with 4.8% of TAC recipients, while perceived quality-of-life improvement also favoured MPA. Nevertheless, these subjective outcomes may reflect expectations and reporting bias where blinding is unclear. Furthermore, functional findings relate specifically to the six available questionnaire items and should not be interpreted as changes in the complete, validated WOMAC instrument.

Local adverse events were infrequent and did not differ significantly between groups. Headache occurred in six TAC recipients and no MPA recipients; however, sparse event counts warrant confirmation using an exact statistical test. Short follow-up and absent post-injection glucose measurements restrict safety conclusions. McAlindon et al. reported greater cartilage loss with repeated TAC injections over two years, underscoring that favourable short-term tolerability cannot establish long-term structural safety. (9)

Study strengths include equal treatment-group sizes, assessment of several clinically relevant outcomes, and adjusted analyses. Limitations

include convenience sampling, uncertain randomisation and blinding, baseline imbalance, incomplete questionnaire data, and absence of a placebo group. A single post-injection assessment prevents determination of onset, duration, or recurrence of symptoms. These limitations restrict generalisability and prevent attribution of all observed improvement to the injected corticosteroid.

Overall, MPA was associated with greater short-term symptomatic improvement in this sample, but confirmation requires randomised, blinded trials with standardised treatment protocols, validated outcome instruments, and repeated follow-up assessments. Injection therapy should remain part of comprehensive management incorporating exercise, weight management, and education, consistent with established recommendations and evidence supporting rehabilitation. Future studies should also distinguish meaningful patient benefit from statistical significance and evaluate uncommon adverse events through systematic monitoring across adequately powered multicentre populations. (4,5)

CONCLUSION

Both MPA and TAC were associated with improvement for knee osteoarthritis in this study of 126 patients with knee osteoarthritis. Conversely, there were large to very large effects whereas MPA produced much larger improvement in VAS pain scores and available 6-item WOMAC/function score, with at least medium to large effect sizes. Those receiving MPA also reported greater satisfaction, greater treatment willingness, and quality-of-life improvements.

The results conform to the literature in which intra-articular corticosteroids are shown to be useful short-term symptomatic treatment options in knee osteoarthritis. By limiting follow-up assessments post-injection to only one point, however, the results do not prove long-term superiority or disease-modifying effects. Therefore, the observed benefit of MPA should be taken as improved short-term clinical response given the conditions of the study. These findings require in

further randomized, blinded, longer-term research utilizing composite validated outcome instruments.

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