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Original Article

# Evaluation of The Efficacy of Intra Articular Methylprednisolone Acetate Injection in Knee Osteoarthritis in A Tertiary Care Center of North India

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## ABSTRACT

**Background**: The purpose of this study was to evaluate the efficacy of intra articular methyl prednisolone acetate injection in knee osteoarthritis using the modified Western Ontario and McMaster University Osteoarthritis index (WOMAC) score and Visual Analogue score. (VAS).

**Methods**: A prospective interventional study on 50 patients (72 knees) with osteo arthritis according to Kellgren and Lawrence radiographic grading were given 80 mg of methylprednisolone acetate intra articular injection and the outcome was assessed using the modified Western Ontario and McMaster University Osteoarthritis index (WOMAC) score and Visual Analogue score. (VAS) prior to the procedure and at 4, 12 and 24 weeks post procedure.

**Results**: The study population consisted of 18 (36.0%) males and 32 (64.0%) females. The mean age of the study population was 61.92±7.37years. 72 Knee Osteo arthritis (KOA) were graded according to Kellgren and Lawrence radiological grading. 29 knees (40.3%) were grade 2, 34 knees (47.2%) were grade 3, and 9 knees (12.5%) were grade 4. The mean WOMAC score and VAS decreased from baseline to 4 weeks, 12 weeks and 24 weeks as demonstrated by the significant p-value at these time intervals. The mean VAS difference between 4 weeks and 12 weeks wasn't statistically significant. (p=0.08) The severity of the KOA significantly correlated with the WOMAC score at baseline, 4 weeks, 12 weeks and 24 weeks. There was an increase in the WOMAC score with severity of KOA grading. There was a significant difference in mean WOMAC score between baseline, 4 weeks, 12 weeks and 24 weeks for all grades of KOA.

**Conclusions**: Intra articular steroid injections remains an easily available, low cost with significant benefits in patients with KOA. Its use can decrease pain, improve functional outcomes and better quality of life up to 24 weeks.

***Keywords****: Intra articular steroid injection, knee osteo arthritis, methylprednisolone acetate, modified Western Ontario and McMaster University Osteoarthritis index score and Visual Analogue score.*

## INTRODUCTION

Osteoarthritis (OA) is a chronic, progressive degenerative disease of the elderly with varying loss of articular cartilage and associated inflammation.[1] The knee joint is most commonly affected followed by hand and hip. [2] Along with pain and deformity, it also results in significant disability and poor quality of life, [3] being ranked as the 11th highest contributor to disability worldwide. [4]

Patients with OA are on a rise, attributed to factors like population expansion, obesity epidemic and increased aging. [5] Due to better diagnostic and healthcare facilities, life expectancy has proportionately increased, further adding to an accumulating socio- economic health burden, increased medical expenses and huge healthcare challenge. [2, 6, 7]

Its aetiology is still unclear, but is considered multi-factorial that includes age, obesity, joint overuse, trauma, mal-alignment, and genetics which leads to progressive OA.[3] The disease affects the whole joint with structural alterations in articular cartilage, subchondral bone, ligaments, capsule, synovial membrane and periarticular muscles. [4]

The pathophysiology of OA is a complex process which includes mechanical, inflammatory and metabolic factors that lead to synovial inflammation, articular cartilage destruction and bone remodelling. [2,3,6] Earlier considerations of "wear and tear passive degenerative process" is now being understood as a dynamic imbalance between repair and destruction of joint tissues , primarily reducing articular cartilage volume ,disturbance in cartilage materials properties and increased susceptibility to mechanical forces.[4] Therapeutic goals of knee Osteoarthritis (KOA) treatment is to reduce pain, preserve mobility, reduce disability, improve patient's quality of life and to slow the progression of disease. [3, 6]

Management starts with conservative treatment using non pharmacological entities like patient education, exercise, weight loss, activity modification, walking aids and physical therapy.[3] Pharmacological treatment advises use of paracetamol (PCM) and non-steroidal anti-inflammatory drugs (NSAID) like ibuprofen, naproxen and diclofenac. Oral NSAID's has been effective in controlling moderate to severe symptoms, but long term use has been associated with gastrointestinal (GI) complications, (peptic ulcer and GI bleeding) renal dysfunction and increased blood pressure which limits their use. [4] Cyclooxygenase 2 inhibitors (COX-2) usage has reduced GI complications but has a higher cost and serious cardiovascular complications. (Myocardial infraction and stroke) [3,4] Next, Intra articular injections (IAI) becomes a viable option in patients who are intolerant to oral medication, when oral drugs become ineffective and patient want to delay or avoid surgery. They include corticosteroids, (CS) hyaluronic acid (HA) as viscosupplementation and orthobiologics like platelet rich plasma (PRP) among many others which can provide short term relief in mild to moderate OA and improve pain and function, thereby delaying the need for total knee replacement which usually is the final treatment for KOA. [5] Studies using different IAI revealed varying levels of pain relief, duration of pain relief, impact on OA progression and cost.[3, 5] Intra articular steroid injection (IASI) is increasing in popularity, its usage documented since 6 decades and advantages of easy delivery, local action and targeting the painful joint, resulting, in a swift and remarkable response with less systemic effect. [8]

Many studies have evaluated the clinical benefits of IASI [6-10]. Evidence from a systematic review and meta-analysis of 15 studies showed a reduction in pain scores and better function at 6 weeks when compared to a placebo.[7] Another meta-analysis demonstrated that patients with severe knee pain at base line will derive more benefits at the short term when IASI are used as compared to patients with less pain at base line. [9] A study using IASI for KOA, showed a reduction in synovial volume and the amount of reduction was correlated directly with the reduction in knee pain and rebound increase in those whose pain relapse [10].

Some studies have raised concerns about chondrotoxicity of IASI in clinical use. [11-13] A study by Pirri et al [11] reported that all CS with the exception of triamcinolone, along with local anaesthetics (excluding ropivacaine and liposomal bupivacaine) exhibited insufficient safety profiles to warrant casual usage in clinical settings. A systematic review by Wernecke et al[12] reported both a dose and time dependant effect of its toxic effect on articular cartilage. Lidocaine, bupivacaine, ropivacaine, levobupivacaine, and mepivacaine were reported to have dose- and time-dependent deleterious effects on chondrocytes that appeared to be made worse by the co- administration of corticosteroids. Ropivacaine at concentrations of 0.5% or less was found to be the least chondrotoxic anesthetic.[13]

Regarding using of IASI in KOA, there are no clear guidelines for its use. The American academy of orthopaedic surgeons[13] (AAOS) states that IASI had considerable evidence with 19 high-quality and six moderate-quality studies supporting the use of intra-articular corticosteroid, although the duration of benefits was often only 3 months. On the other hand the American college of Rheumatology/ Arthritis foundation guidelines [14] report that trials using IASI have demonstrated short-term efficacy in KOA and strongly recommend in hip and KOA.

Methyl prednisolone acetate, (MPA) is a commonly used synthetic glucocorticoid with higher intra cellular steroid receptor affinity, potent anti-inflammatory and immunosuppressive effect by a complex mechanism of action that has a multifocal effect on immune cascade, reducing vascular permeability at a cellular level and inhibits accumulation of inflammatory cells thereby blocking the secretion of inflammatory mediators like prostaglandins and leukotriene's which is the treatment rationale to reduce pain and swelling within joint. [3,4,6]

There is conflicting data regarding the effectiveness of IASI in KOA with treatment outcomes varying from no efficacy or slight improvement in pain and joint function for a small duration to relief of pain for few or several weeks. [15-17]

Inspite of such conflicting data and lack of uniformity for IAI recommendations, their use in clinical practice is constant and growing, most likely due to limited options for pain management. [5] Evidence of efficacy is not the only reason for utilizing a particular regimen in clinical practice. Cost and availability becomes a decisive factor, especially in developing countries which are often populous, with scarce financial and economic resources in an overburdened health system. Hence,

we should be judicious in maximizing health benefits, utilizing to the best of our ability our resources within a limited health budget system and search for alternative treatment options that can alleviate pain and improve function in KOA and postpone surgery as far as possible.

The purpose of this study was to assess the efficacy of intra articular methyl prednisolone acetate injection in KOA in the Indian population using the Modified Western Ontario and McMaster Universities Osteoarthritis Index (WOMAC) score and visual analogue score. (VAS)

**MATERIAL AND METHODS:**

This prospective interventional study was conducted on 50 consenting patients visiting the orthopaedics outpatient department from December 2020 to May 2021 and fitting the inclusion criteria. The inclusion and exclusion criteria are given in supplementary table 1. Written informed consent was obtained from all patients. After approval from the Institutional Ethics committee, a detailed history and examination of affected knee joint was done for all patients and recorded in a case record form. All standing antero- posterior and lateral knees x-rays were graded for OA using Kellgren & Lawrence (KL) radiographic grading[18] Before procedure, patient functional assessment was done using Modified Western Ontario and McMaster Universities Osteoarthritis Index (WOMAC) score[19], pain was evaluated using Visual Analogue Score. (VAS) Lignocaine sensitivity and blood sugar estimation was done prior to the procedure. Under full aseptic precautions in minor operation theatre, IASI was reconstituted using 8ml of 2% lignocaine and 2 ml (80 mg) of MPA and injected through the supero -lateral patella approach into the knee joint. Sterile dressing was done at the injection and patient was reviewed at 4$^{th}$, 12$^{th}$, and 24weeks post procedure .WOMAC and VAS score was assessed during follow up and recorded and compared with pre procedure baseline scores.

The data was entered into the Microsoft excel and the statistical analysis was performed by statistical software SPSS (Statistical Package for Social Sciences) version 25.0. The quantitative (numerical variables) were present in the form of mean and Standard Deviation (SD) and the qualitative (categorical variables) were present in the form of frequency and percentage. The student t-test was used for comparing the mean values between the 2 groups whereas the chi-square test was applied for comparing the frequency. The p-value was considered to be significant when less than 0.05.

**RESULTS:**

The study population consisted of 18 (36.0%) males and 32 (64.0%) females. Among the study population, 24 patients (48.0%) belonged to 51-60 years, 21patients (42.0%) belonged to 61-70 years and 5 patients (10.0%) belonged to above 70 years. The mean age of the study population was 61.92±7.37years. The minimum age was 50 years and maximum age was 78 years. 22 patients (44%) had bilateral involvement and 28 patients (56%) had unilateral involvement. 72 KOA were graded by KL radiological grading. 29 knees (40.3%) were grade 2, 34 knees (47.2%) were grade 3, and 9 knees (12.5%) were grade 4.

The mean WOMAC score was compared at different time intervals between baseline, 4 weeks, 12 weeks and 24 weeks using the repeated measures ANOVA test. (Table 1). The mean WOMAC score at Baseline was 79.48±7.83, 4 weeks was 64.26±7.72, 12 weeks was 61.27±7.82 and 24 weeks was 56.22±10.06. (Figure I)There was a significant difference in mean WOMAC score between baseline, 4 weeks, 12 weeks and 24 weeks.

The inter time interval comparison of mean WOMAC score was done using the post-hoc Bonferroni test. (Table 2) There was a decline in the WOMAC score as demonstrated by the significant p-value at different time intervals.

The mean VAS score was compared between different timelines (baseline, 4 weeks, 12 weeks and 24 weeks) using the repeated measures ANOVA test**.** (Table 3)The mean VAS score at Baseline was 7.18±1.22, 4 weeks was 4.65±1.57, 12 weeks was 3.61±1.53 and 24 weeks was 2.78±1.41. (Figure II) There was a significant difference in mean VAS score between baseline, 4 weeks, 12 weeks and 24 weeks.

The inter time interval comparison of mean VAS was done using the post-hoc Bonferroni test. (Table 4) The mean VAS score decreased significantly from baseline to 4 weeks to 12 weeks and to 24 weeks. The difference between 4 weeks and12 weeks wasn't statistically significant. (p=0.08)

The severity of the KOA significantly correlated with the mean WOMAC score (Table 5) at baseline, 4 weeks, 12 weeks and 24 weeks. There was an increase in the WOMAC score with severity of the KOA as demonstrated on bivariate analysis. The mean WOMAC score for each grade of OA was calculated at baseline, 4 weeks, 12 weeks and 24 weeks and compared using the repeated measures ANOVA test. There was a significant difference in mean WOMAC score between baseline, 4 weeks, 12 weeks and 24 weeks for all grades of KOA. (Figure III)

The inter time interval comparison of difference in fall in WOMAC scores between grades of KOA in different time intervals (table 6) was done using the post-hoc Bonferroni test. The mean WOMAC score decreased significantly from

baseline to 1 week to 4 weeks to 12 weeks to 24 weeks for all grading of OA. The mean VAS for a particular grade of OA was compared over different time lines (table 8) was done using the post-hoc Bonferroni test**.** There was statistically significant improvement of VAS over time lines for all grades of OA.

**Table 1: Mean WOMAC scores at different time intervals**

| WOMAC score | Mean | Standard. Deviation(SD) | F-value | p-value |
|---|---|---|---|---|
| **Baseline(pre procedure)** | 79.48 | 7.83 | 21.156 | < 0.001* |
| **4 weeks** | 64.26 | 7.72 | | |
| **12 weeks** | 61.27 | 7.82 | | |
| **24 weeks** | 56.22 | 10.06 | | |

**Table 2: Comparison of mean WOMAC score at different inter-time intervals**

| Comparative timelines | | Mean WOMAC score Difference | p-value |
|---|---|---|---|
| **Baseline** | **4 weeks** | 15.22 | 0.05* |
| **Baseline** | **12 weeks** | 18.21 | <0.001* |
| **Baseline** | **24 weeks** | 23.26 | < 0.001* |
| **4 weeks** | **12 weeks** | 2.99 | 0.003* |
| **4 weeks** | **24 weeks** | 8.04 | < 0.001* |
| **12 weeks** | **24 weeks** | 5.05 | 0.01* |

**Table 3: VAS at different time intervals**

| VAS score | Mean | Std. Deviation | F-value | p-value |
|---|---|---|---|---|
| **Baseline** | 7.18 | 1.22 | 32.898 | < 0.001* |
| **4 weeks** | 4.65 | 1.57 | | |
| **12 weeks** | 3.61 | 1.53 | | |
| **24 weeks** | 2.78 | 1.41 | | |

**Table 4: Comparison of mean VAS e at different inter time intervals**

| Comparative timelines | | Mean Difference | p-value |
|---|---|---|---|
| Baseline | 4 weeks | 2.53 | 0.03* |
| Baseline | 12 weeks | 3.58 | < 0.001* |
| Baseline | 24 weeks | 4.40 | < 0.001* |
| 4 weeks | 12 weeks | 0.7 | 0.08 |
| 4 weeks | 24 weeks | 1.87 | 0.006* |
| 12 weeks | 24 weeks | 0.8 | 0.1* |

**Table 5: WOMAC scores in different time lines in comparison with grades of OA**

| WOMAC score | Baseline | 4 weeks | 12 weeks | 24 weeks | F-value | P Value |
|---|---|---|---|---|---|---|
| **OA2** | | | | | | |
| Mean | 74.06 | 62.69 | 60.13 | 55.21 | 83.785 | < 0.001* |
| Std. Deviation | 6.9 | 7.42 | 7.59 | 9.12 | | |
| **OA3** | | | | | | |
| Mean | 80.22 | 64.24 | 61.57 | 57.08 | 21.527 | < 0.001* |
| Std. Deviation | 6.85 | 7.45 | 7.29 | 9.64 | | |
| **OA4** | | | | | | |
| Mean | 86.82 | 70.64 | 67.48 | 63.33 | 37.554 | < 0.001* |
| Std. Deviation | 4.43 | 8.08 | 8.85 | 11.41 | | |

**Table 6- Comparison of difference in fall in WOMAC scores between grades of OA at different inter time intervals**

| WOMAC | Baseline- 4 weeks | Baseline- 12 weeks | Baseline- 24 weeks | 4weeks -12 weeks | 4weeeks -24 weeks | 12weeks -24 weeks |
|---|---|---|---|---|---|---|
| **OA 2** | | | | | | |
| **Mean Difference** | 11.37 | 13.93 | 18.85 | 2.56 | 7.48 | 4.92 |
| **p-value** | < 0.001* | < 0.001* | < 0.001* | < 0.001* | < 0.001* | < 0.001* |
| **OA3** | | | | | | |

| | | | | | | |
|---|---|---|---|---|---|---|
| **Mean Difference** | 15.98 | 18.65 | 23.14 | 2.67 | 7.15 | 4.49 |
| **p-value** | < 0.001* | < 0.001* | < 0.001* | < 0.001* | < 0.001* | < 0.001* |
| **OA4** | | | | | | |
| **Mean Difference** | 16.18 | 19.33 | 23.49 | 3.15 | 7.3 | 4.15 |
| **p-value** | < 0.001* | < 0.001* | < 0.001* | 0.045* | < 0.001* | < 0.001* |

**Table 7: Comparison of mean VAS score & grades of OA at different time intervals**

| VAS score | Baseline | 4 weeks | 12 weeks | 24 weeks | F-value | P-Value |
|---|---|---|---|---|---|---|
| **OA grade 2** | | | | | | |
| **Mean** | 6.91 | 4.31 | 3.29 | 2.79 | | |
| **Std. Deviation** | 1.37 | 1.55 | 1.55 | 1.32 | 30.29 | < 0.001* |
| **OA grade 3** | | | | | | |
| **Mean** | 7.28 | 4.75 | 3.65 | 2.81 | | |
| **Std. Deviation** | 1.14 | 1.57 | 1.41 | 1.29 | 33.19 | < 0.001* |
| **OA grade 4** | | | | | | |
| **Mean** | 7.55 | 5.42 | 4.7 | 3.97 | | |
| **Std. Deviation** | 1.09 | 1.44 | 1.55 | 1.91 | 73.747 | < 0.001* |

***- statistically significant**

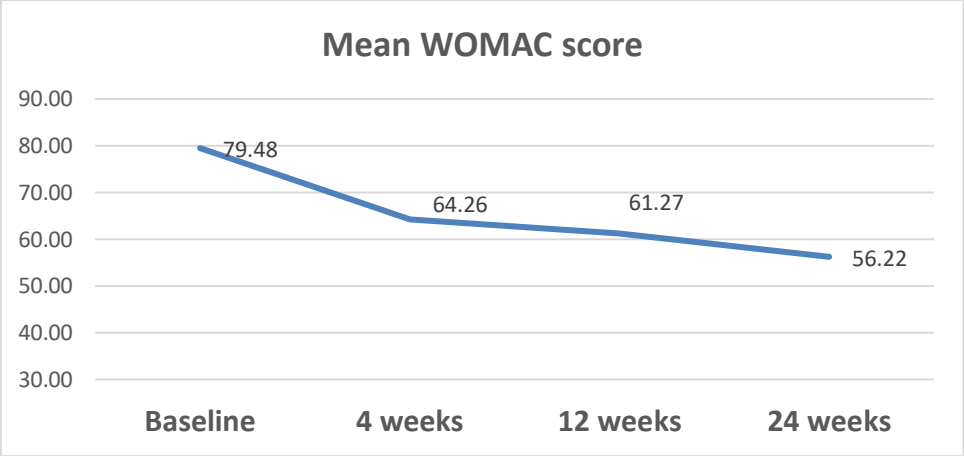


**Figure I: Mean WOMAC scores at different time intervals**

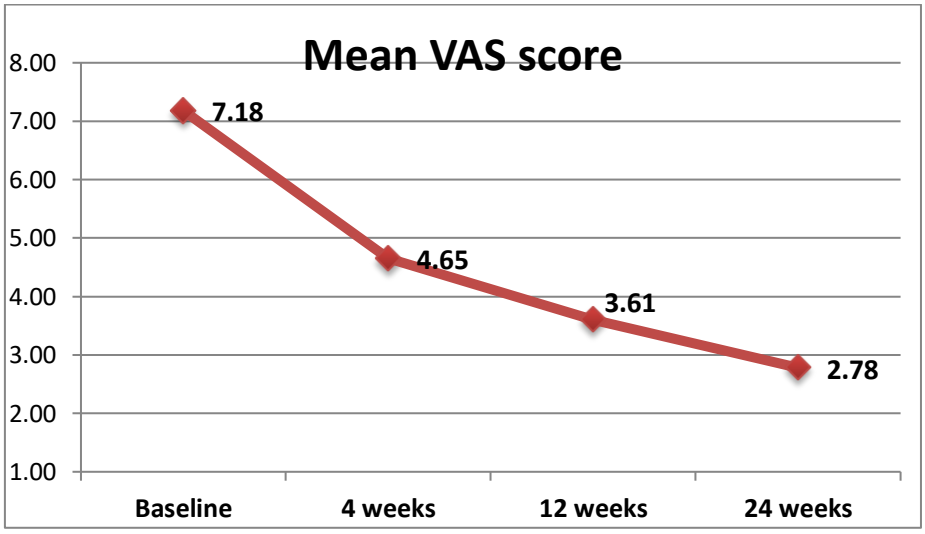


**Figure II: Comparison of VAS at different time intervals**

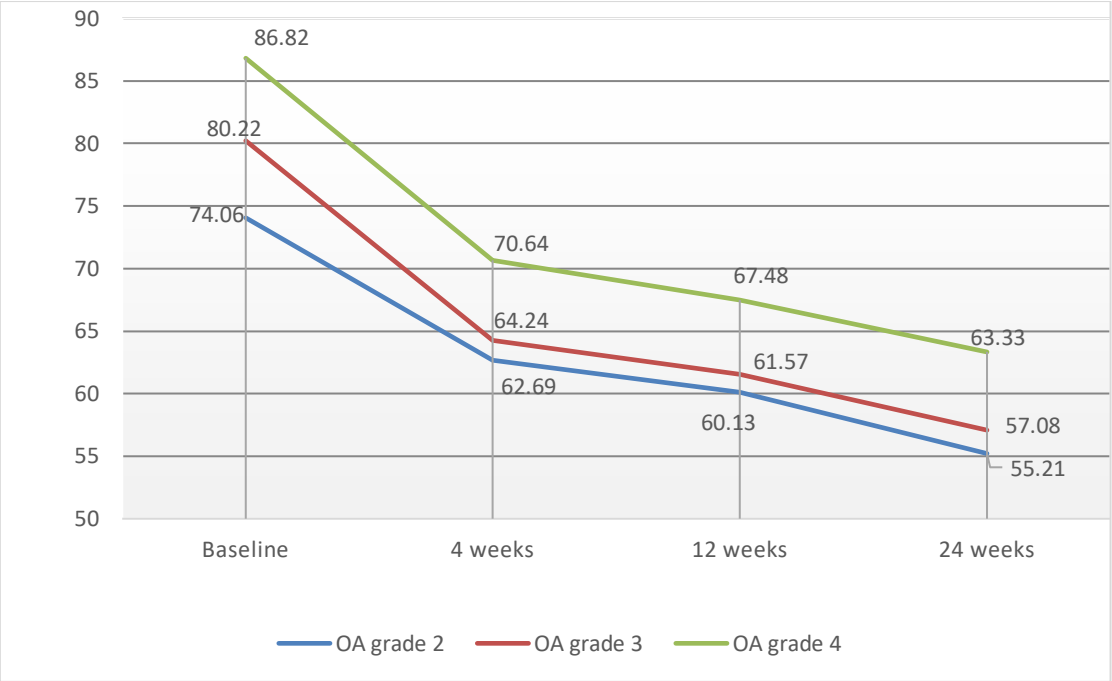


**Figure III: WOMAC scores- Comparison between grades of OA**

**Supplementary table 1**

| Criteria | Details |
|---|---|
| Inclusion | Males and females age more than 50 years with primary osteo arthritis of knee. |
| | Knee pain ≥ 6 weeks. |
| | KL Grade ≥2 OA knee. |
| | Diagnosed with primary OA knee. |
| | Failure of at least one conservative treatment regimen (e.g. physical therapy, analgesics). |
| | Ambulatory patient. |
| **Exclusion** | Secondary inflammatory disease (Rheumatoid arthritis, Reiter's syndrome, psoriatic arthritis, gout, ankylosing spondylitis). |
| | Uncontrolled diabetes. |
| | Untreated symptomatic injury of knee (e.g., acute traumatic injury, cruciate ligament Injury/collateral ligament injury). |
| | Use of systemic immunosuppressant within 6 weeks of screening. |
| | Patients not consenting for treatment. |

## DISCUSSION

KOA is a significant problem worldwide and most prevalent form of arthritis causing pain and loss of function. IAI using HA, PRP and CS have been used for short term relief in patients suffering from KOA with varying results. Both HA and PRP injection have the downside of being more expensive than CS injection and thus imposes greater financial burden upon the patient.[5] This fact becomes more pressing in resource scarce country like India, where OA knee afflicts a large swathe of people who are economically weak and can't afford costly injections. Orthobiologics is a newer and evolving modality of research in treatment of KOA.[3, 5, 20] In recent years, there has been an explosive increase in number of available therapies of which PRP is the fore runner, garnishing a lot of academic interest. The debate regarding use of PRP in KOA still continues with conflicting evidence. A meta-analysis of 27 randomised controlled trials (RCT) of level 1 evidence wherein PRP was used in KOA showed that PRP outperformed HA and placebo in terms of pain and patient reported outcomes. [21]

Laver et al in a review of 48 RCT showed that 38 studies reported that PRP was superior to other injections including CS, HA and saline whereas 10 studies showed no difference in treatment modalities which was attributed to heterogeneous preparations and varying methodology.[21]

Besides understanding IAI, its usage and their varying efficacy supported by academic evidence, another important consideration is the cost of treatment as well as its benefit to risk ratio. In a highly populous country like India where health care resources and finance is limited, cost effectiveness of treatment is paramount. Also, most of the evidence based studies

have been conducted and interpreted from other parts of the globe with no studies being reflective of the Asian population that mirrors a unique genetic pool that indulge in a very different personal, social and religious life style from the rest of the western world .

Hence we undertook this study using a low cost, easily available corticosteroid (MPA) to assess the clinical and functional outcomes in KOA in Indian sub-continent.

In our study, the mean age of the study population was 61.92±7.37 (50-78) years, similar to the findings by Nalini et al [22] who reported that the mean age was 59.20±11.19 years with the age range of 56–65 years (36.66%) being the most common. Sampath et al [1] reported the age range of the study population was 58-84 years with a mean 67 years. In our study, according to KL grading, majority (56.0%) of the study participants were in grade 3 OA followed by 32.0% study participants in grade 2 OA and 12.0% patients in grade 4 OA. In our study, the mean WOMAC score at baseline was 79.48±7.83, at 4 weeks was 64.26±7.72, at 12 weeks was 61.27±7.82 and at 24 weeks was 56.22±10.06. There was a decline in the WOMAC score as demonstrated by the significant p-value at different time intervals. These findings were similar to other authors like Khongwir, Matzkin, and Raynauld et al respectively. Khongwir et al [23] reported a mean baseline WOMAC score is 71.2±5.22, at 2 months 60.4±8.00, at 4 months 66.93±9.40 and at 6 months follow up was 73. 86±6.25 (p=0.00001). The best effect was reported at 2 months with effects decreasing at 4 and 6 months. Matzkin et al [24] found significantly improved WOMAC scores at 3, 6, 12, and 24 weeks after injection. Those with worse arthritis (KL grade 3 or 4) had statistically significant poorer scores at 6 weeks after injection (P = 0.028) and 3 months after injection (P = 0.004), although they showed improvement from baseline. Raynauld et al [25] performed a study for evaluating the safety and analgesic efficacy of Triamcinolone in patients suffering from knee osteoarthritis using WOMAC scale. They noted significant improvement in KOA stiffness and pain, without any deleterious effect on knee structures. A study by Sampath et al [1] were contrary to our findings, wherein he reported that though VAS decreased, Knee Society Score (KSS) did not decrease significantly in patients with KOA after IASI. Smith et al [26] in an RCT compared IASI with arthroscopic lavage versus only arthroscopic lavage as placebo, and observed that there was better response in corticosteroid group at 4 weeks, however there was no difference beyond that period, pointing at short term effectiveness of IASI. Similarly, Bellamy et al [27] showed that IA- MPA could reduce pain but were generally short-acting**.** Maricar et al [28] found that 73.4% patients responded to treatment in the short term of 2 weeks and 20.1% in the long term at 6 months after injection. This was in contrast with our study which found statistically significant improvement in WOMAC scores till 24 weeks of follow up across all grades of KOA. Beyond 24 weeks the exact duration of the effect of corticosteroids could not be ascertained as our study was limited to a 24 week follow up timeline. Findings by Shikhar et al [29] compared IAI using triamcinolone acetonide (TA) and MPA revealed WOMAC score at 12 weeks follow-up was comparable between the groups. He concluded that long term treatment of KOA with IASI at repeated interval appeared to be clinically effective in reducing symptoms. A similar study of comparison using the same molecules by Syam et al [30] found that KSS of TA group improved to a mean of 75, 71, 65 and 60 from the baseline score of 55 on day 0, 1st month, 3rd month and 6th month respectively. Similarly, the KSS of the MPA group improved to a mean of 74, 72, 64 and 59 from the baseline score of 57 on day 0, 1st month, 3rd month and 6th month respectively. Yavuz et al [31] study further corroborates the findings of Shikhar et al and Syam et al and indicates that the beneficial effects of IA-MPA injections could last as long as 24 weeks.

In the current study, the mean VAS score decreased significantly from Baseline (7.18±1.22) to 4 weeks (4.65±1.57) to 12 weeks (3.61±1.53) to 24 weeks (2.78±1.41). There was a decline in the VAS score as demonstrated by the significant p-value at different time intervals. The effect of corticosteroids in decreasing pain is well established in literature. Nalini et al [22] found that the mean VAS before IAI was 9.37±0.80 and after administering IA- MPA, the mean VAS at 2 weeks and 24 weeks was 2.70±1.62 and 0.80±1.21 respectively. In a comparative study conducted by Kumar et al, [32] where IA-MPA was compared with IA- triamcinolone acetonide (TA) for KOA, concluded that both groups had significant decline in pain and swelling. Buyuk et al [33] demonstrated that both IA- TA and MPA are effective at reducing pain and improving function in patients with KOA, and their efficacy may last up to 24 weeks.

Pyne et al [34] reported that TA was statistically more efficient in pain relief 3 weeks after injection than MPA while Yavuz et al [31] disagreed and stated that MPA was statistically more effective in relieving pain than other agents including triamcinolone until 6 weeks after injection. Our study results agrees with findings reported by Singh et al [35] and Yratapalli et al, [36] where all patients reported significant decrease in VAS score following IASI and the effect was evident till last follow up (24 weeks).

Inspite of the apparent benefits of IASI, serious long term side effects like cartilage, synovium and bursa damage can occur with prolonged usage thereby further worsening of the pathological process within the knee and thereby increasing pain .[6, 11 ,12, 20] The safety of IASI has been also addressed in two RCT's [16,25] which assessed the safety and efficacy in use (at 2 years) for knee pain related to OA and concluded that repetitive IASI appear to be safe, besides providing affordable pain relief. Jain et al [37] found that MPA provided immediate and prolonged improvement in pain, stiffness and joint function, and has a safe profile. In contrast, studies by Bellamy et al [27] and Juni et al [38] reported the effect of IASI to be relatively short lived with minimal or no pain relief beyond 4-24 weeks of treatment. We did not encounter any complications during

the study period. Overall, IASI in KOA is relatively safe for short-term period and is recommended to be used as short term solutions in acute flare ups in KOA.

**LIMITATIONS OF THE STUDY**

The limitations of the present study are small sample size, single-centred study, not compared with drugs of similar efficacy and long-term outcomes not studied. Hence, further study may be done with a large population, multicentre comparative study with long-term follow-up.

**CONCLUSION:**

This study reinforces that IASI remains a viable option in patients with KOA having acute flare-ups, who want to postpone surgery or do not want surgery at all. Its use can decrease pain, improve function and quality of life, albeit temporarily and also decrease the use of harmful pain medication with chronic use. In a highly populous country like India, where finance and medical resources are constrained, IASI it is a cost effective, easily available and relatively simple treatment option along with it being a useful adjunct to physical therapy, to effectively and safely manage chronically painful KOA.

**CONFLICT OF INTREST**: none

**FUNDING SOURCE**: none

**ETHICAL APPROVAL**: This study was approved by the institutional ethical committee with certificate no: SU/SMS&R/76-A/2020/109.

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