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EFFICACY OF INTRA-ARTICULAR INJECTION OF METHYLPREDNISOLONE ACETATE AND TRIAMCINOLONE ACETONIDE IN PRIMARY KNEE OSTEOARTHRITIS: A RANDOMIZED, DOUBLE BLINDED, INTERVENTIONAL STUDY.

Anaesthesiology

Dr Sanjiv Bansal

Dr Jyoti Mourya* *Corresponding Author

Dr Rajeev Sharma

ABSTRACT

Introduction: Osteoarthritis is a degenerative joints disease and an important cause of disability among elderly with management ranging from non-pharmacological measures, intra-articular injections to surgery. Objective of this study was to compare pain relief (VAS Score) and Functional ability (LFI score) between intra-articular injection of Methylprednisolone and Triamcinolone in primary knee osteoarthritis.

Material And Methods: A hospital based, double blinded, Randomized interventional study was conducted on 84 cases aged 45 – 75 years with primary Knee OA, Kellgren-Lawrence classification Radiological grade 2 and above randomized to receive intra-articular injection of either Methylprednisolone or Triamcinolone. Pain (VAS) score and functional ability (LFI score) were evaluated on Day 3, week 1, 6 and 12.

Results: Both VAS score and LFI score improved significantly in both groups at all follow up upto 12 weeks. VAS score was significantly lower in Methylprednisolone group at 3 day, 1 week, 6 week and 12 week as compared to Triamcinolone group. No significant difference was seen in LFI score between the two groups at any follow up time.

Conclusion: Intra articular steroid injection can be used as effective non surgical measure in osteoarthritis, especially for short term relieve with Methylprednisolone being more effective in reducing pain upto 12 weeks.

KEYWORDS

Osteoarthritis, Methylprednisolone, Triamcinolone, intra-articular injection, Knee

INTRODUCTION:

Osteoarthritis (OA) is a degenerative disease of joints that causes restriction of activity of daily living.[1] Worldwide 9.6% of men and 18.0% of women over age of 60 years have symptomatic osteoarthritis. Approximately 80% of those with OA have limitations in movement, and 25% cannot perform their major activities of daily life.[2] It is an important cause of disability and the fourth leading cause of years lived with disability.[3] Treatment cost is also high for such long duration and progressive disease.[4,5] In India, approximately 40% population above 70 years shows OA, in which nearly 2% have severe knee pain and disability.[6] The pain and decreased function associated with OA place a major burden on communities as well as health and social care systems.[7]

Osteoarthritis result from failure of chondrocytes to maintain homeostasis between synthesis and degradation of extracellular matrix,[8] and a low grade inflammation contributing to structural disease progression.[9,10] Objectives of OA management are to reduce the level of pain, reduce inflammation, slow cartilage degradation, improve function and reduce disability.[8]

The recommended hierarchy of treatment is non-pharmacological treatments first, followed by pharmacological treatment and then surgery.[11] Non-pharmacological treatment includes physical therapy, weight loss, orthotic devises, Pulsed electromagnetic field therapy, Transcutaneous electrical nerve stimulation (TENS) etc. Pharmacological Treatment includes NSAIDS, opioid analgesics, psychotropic drugs, intra-articular treatment injections of corticosteroids, hyaluronans and tidal irrigation. Surgical approach including arthroscopy, osteomy, uni-compartmental knee replacement and total knee arthroplasty are the last option.[12]

Treatment with corticosteroids injected directly into the joint has been shown to be effective, especially in OA of the knee and can be the last non-operative modality that can be performed[13,14].Intra-articular steroidal injection provides pain relief by the prostaglandins synthesis inhibition and controls local inflammation by decreasing the activity of collagenase and others destructive enzymes.[15] It also leads to increase in relative viscosity of the synovial fluid with an increase in hyaluronic acid (HA) concentration[16,17] The American College of Rheumatology (ACR), the Osteoarthritis Research Society International, and the European League against Rheumatism recommend the use of intra-articular corticosteroids for short-term acute pain relief in OA owing to their anti-inflammatory and immunosuppressive effects.[12,18,19] and is directly targeted at the affected joint with few systemic effects.[20,21] Clinically, it causes decrease in erythema, swelling, heat and tenderness of the inflamed joints.

Various studies have been conducted to compare different types of corticosteroids for intra-articular injection in OA but inconsistent results are available.[22-25] Moreover, not much literature is available on effect on quality of life. This study aimed to compare the efficacy of two intraarticular corticosteroid injections (Methylprednisolone and Triamcinolone) in terms of symptomatic pain relief (VAS Score) and functional state (LFI Score) of the patients having knee osteoarthritis.

MATERIAL AND METHODS:

A hospital based, randomised, double blinded, interventional study was conducted in the Pain Clinic, Department of anaesthesiology of a tertiary care centre of Northern India during December 2018 to May 2019. A total of 84 cases aged 45 – 75 years, of either gender presenting to the knee clinic with a diagnosis of primary Knee OA, Kellgren - Lawrence classification Radiological grade 2 and above and Pain severity of ≥ 5 VAS score (0-10 Likert scale) were included in the study. Sample size was calculated at 95% confidence & 80% power to verify the expected difference of 1.1 (±1.2) in change in VAS score from baseline to 12 weeks post injection in both groups.

Secondary arthritis (Post trauma, post surgery, rheumatoid, tubercular, psoriatic, haemophilic), Patients who were administrated intra-articular steroid in last 3 months, Patients with serious concomitant medical disease (uncontrolled hypertension, uncontrolled Diabetes mellitus, chronic renal failure and any disease related to bone and joint), Patients on immunosuppressive drugs, anticoagulant treatment, or systemic steroids and patients who planned to undergo knee surgery for next 12 weeks were excluded from the study.

Study was started after permission from the institutional ethical committee. Eligible subjects coming to pain clinic were recruited consecutively and were randomized into two groups using block randomization method. Neither the injecting doctor nor the patient knew about the drug been injected (double blinding). The injection was prepared by a separate doctor who was unaware of which patient it would be given to. All patients were subjected to standard pre injection check up and routine investigations including bilateral knee X ray. A uniform anaesthetic technique was undertaken in all patients. All of the injections were administrated by the same investigator in the aseptic setting, and the injection site was bandaged using same procedure and was followed for one hour. The more painful knee was chosen in the patients with bilateral knee osteoarthritis. Under all aseptic conditions, ultrasound guided (sonosite micromaxx-linear probe 6-13 MHz) intra-articular injection was given in knee joint with knee flexed at 90°.

Group A: Intra-articular injection of Triamcinolone acetonide 80 mg/2 ml.

Group B: Intra-articular injection of Methylprednisolone acetate 80 mg/2 ml.

On injection site gauze and bandage were applied and advised rest for 2 days. Subsequently patient was called for follow-up visits on the Day 3. VAS & LFI scores were noted & any signs of systemic disease ruled out. Similar Knee physiotherapy was advised to all patients and clinical evaluation was done on 1st, 6th and 12th week. Written informed consent was obtained from all patients prior to initiation of study. VAS Score (on a scale of 1 – 10) was used to assess pain and LFI SCORE (Lequesne functional index) [26-28] was used to assess functional level of all patients. LFI score evaluates 3 index including pain, maximum distance walked and activities of daily living. LFI score varies from minimum 0 to a maximum of 24.

Statistical Analysis:

Continuous variables were expressed as mean and standard deviation and analysed using unpaired t test. Categorical variables were expressed as proportion and analysed using chi square test. Ordinal data was expressed as median and inter quartile range (IQR) and analysed using Mann Whitney rank sum test for intergroup comparison and Friedman test for within-group comparison with post hoc analysis by Wilcoxon signed rank test using Bonferroni adjustment. P value <0.05 was considered as significant. All statistical analyses were done using SPSS software.

Results:

Both the group were comparable in relation to their baseline characteristics (Table 1). Most of the subjects in both groups were aged 55 – 65 years. VAS score was significantly lower in Methylprednisolone group at 3 day, 1 week, 6 week and 12 week as compared to Triamcinolone group. Change in mean VAS score in both groups from baseline to 12 weeks was statistically significant (Table 2). Highest improvement was seen at day 3 from baseline in both groups and this decrease in pain was maintained till week 6. At 12 week follow up there was slight increase in VAS in both groups, but was still lower in Methylprednisolone group (Figure 1). Post hoc analysis showed significant improvement at all follow up times except from Day 3 to week 1 in both groups. There was statistically significant decline in LFI score from baseline to 12 weeks in both groups ($p<0.001$), however at any point no significant difference was seen between the two groups (Table 3 & Figure 2). Post hoc analysis showed significant improvement at all follow up times except from Day 3 to week 1 in both groups.

Table 1: Baseline Characteristics Of Study Groups

Characteristics	Group A	Group B	P value
Age (years)	62.07 ±5.69	60 ±6.55	0.126
Gender – Male - Female	19 (45.24%) 23 (54.76%)	12 (28.57%) 30 (71.43%)	0.175
Weight (Kg)	70.9 ±7.52	68.88 ±8.34	0.248

Table 2: Comparison Of VAS Score At Different Follow Up Time

Time	Group A		Group B		P value[2]
	Mean ± SD	Median (IQR)	Mean ± SD	Median (IQR)	
Baseline	6.55±0.80	7 (6,7)	6.74 ±0.86	7 (6,7)	0.426
Day 3	1.64±0.82	2 (1,2)	1.17 ±0.69	1 (1,2)	0.005(S)
Week 1	1.64±0.82	2 (1,2)	1.167 ±0.70	1 (1,2)	0.005(S)
Week 6	1.79 ± 1.0	2 (1,2.25)	1.24±0.69	1 (1,2)	0.008(S)
Week 12	2.38± 1.06	2 (2,3)	1.81 ±0.97	2 (1,2)	0.013(S)
P value[1]	<0.001 (S)		<0.001 (S)		

[1]p value calculated using Friedmann test
[2]p value calculated using Mann Whitney Rank sum test

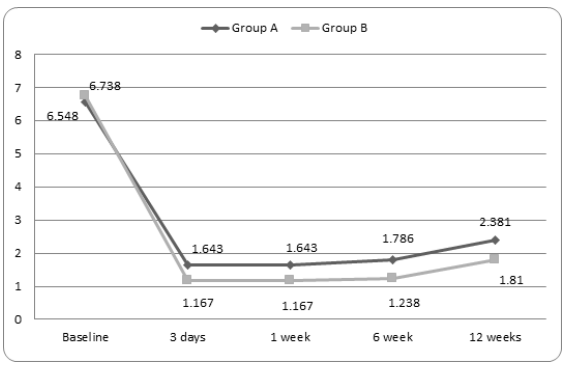

Figure 1: Mean VAS Score Of The Study Groups

Table 2: Comparison Of LFI Score At Different Follow Up Time

Time	Group A		Group B		P value[2]
	Mean ± SD	Median (IQR)	Mean ± SD	Median (IQR)	
Baseline	16.18±1.56	16 (15,17.2)	16.25±1.04	16.3 (15.5,17.2)	0.549
Day 3	5.04±1.04	5 (4,6)	4.85±1.20	4 (4,6)	0.368
Week 1	5.06± 1.04	5 (4,6)	4.85±1.26	4 (4,6)	0.306
Week 6	5.32 ± 1.22	5.25 (4,6.5)	5.02 ±1.48	4.5 (4,6)	0.198
Week 12	6.18± 1.49	6 (5,7.125)	5.77 ±1.73	6 (4,7)	0.209
P value[1]	<0.001 (S)		<0.001 (S)		

[1]p value calculated using Friedmann test
[2]p value calculated using Mann Whitney Rank sum test

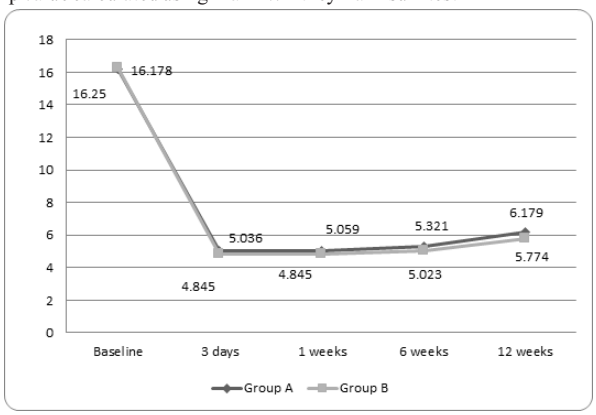

Figure 2: Mean LFI Score In Both Groups

DISCUSSION:

Intra-articular injection of steroids constitutes a successful component of non operative management of OA. In present study, intra-articular corticosteroids injection significantly improved VAS score. Mean VAS score at 1 week was significantly lower in Methylprednisolone Group (1.17±0.69) as compared to Triamcinolone Group (1.64± 0.82). In a similar study by Yavuz U et al [29], Methylprednisolone was found to be more effective than Triamcinolone at 1 week in their study was similar to ours ($p<0.005$).

At 6 weeks follow up the mean VAS score of Methylprednisolone group (1.24 ±0.69) was significantly lower as compared to Triamcinolone group (1.79 ± 1.00). In a similar study of Yavuz U et al [29] also the score mean VAS score of Methylprednisolone group (4.3±1.4) was lower as compared to Triamcinolone Group (5.2±1.2), however the difference was not statistically significant. This higher VAS score might be due to higher baseline VAS score in study of Yavuz U et al [29] as compared to our study.

At 12 weeks mean VAS score of Methylprednisolone group was significantly lower (1.81 ±0.97) as compared to Triamcinolone Group (2.38± 1.06). VAS score was also found to be lower in study by Yavuz U et al [29](5.0±1.3 vs 5.7±1.5), Syam NSH et al [30](4.4 vs 4.7), Buyuk AF et al [31] (5.2 ± 2.4, Jain P et al [32] (4.47 ± 1.16 vs 4.98 ± 1.23). Though these studies did not find these differences to be statistically significant, VAS score was lower in Methylprednisolone group.

In our study we observed that there was significant amount of improvement in pain after intra articular injection in both Methylprednisolone and Triamcinolone group from baseline to 12 weeks in agreement with the findings of study by Lomonte AB et al [22] and Buyuk AF et al [31]. In our study Methylprednisolone was found superior in improving pain VAS score as compared to Triamcinolone similar to findings of studies like Jain P et al [32]. Buyuk AF et al [31] and Kumar A et al [33] concluded that both intra-articular Triamcinolone and Methylprednisolone have similar efficacy in relieving pain ($p>0.05$). Debasish Pyne et al [34] study concluded that both steroid injections led to significant improvement in VAS at week 3 compared to baseline, but only Methylprednisolone maintained significant benefits at week 8.

At 1 week follow up the mean LFI score for Methylprednisolone group (4.85±1.26) was lower than Triamcinolone group (5.06± 1.04). Yavuz

U et al [29] also reported lower LFI score in Methylprednisolone group (8.4±3.2 vs 9.9±3.0), though the difference was not statistically significant. At 6 week also the mean LFI score for Methylprednisolone group (5.02 ±1.48) was lower as compared to Triamcinolone group (5.32 ± 1.23). Yavuz U et al [29] also reported lower LFI score in Methylprednisolone group (10.1±3.1 vs 11.3±3.4), though the difference was not statistically significant. Even at 12 weeks follow up the mean LFI score for for Methylprednisolone group was lower (5.77 ±1.74) as compared to Triamcinolone group (6.18± 1.49) Yavuz U et al [29] also reported lower LFI score in Methylprednisolone group (11.3±3.5 vs 12.0±3.4),

Both the drugs were found to significantly lower LFI score in present study with no difference between the two. In a similar study Debasish Pyne et al's [34] concluded that both steroid injections gave a significant improvement in LFI at week 3 compared to baseline, with no significant difference between them.

CONCLUSION:

Both Triamcinolone Acetonide and Methylprednisolone Acetate significantly relieve pain sustained upto 12 weeks. Methylprednisolone was more effective in reducing pain as compared to Triamcinolone at upto 12 weeks and may be even longer. Functional quality (LFI score) also significantly improved with time with both steroids with no significant difference between them. Intra articular steroid injection, especially Methylprednisolone can be used as effective non surgical measure in osteoarthritis, especially for short term relieve. Further studies with longer follow up period could better establish efficacy and superiority of these drugs.

Conflict of Interest: None
Acknowledgement:

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