Original Research Article

Outcome of intra-articular corticosteroid vs. intra-articular ketorolac in symptomatic knee osteo-arthritis: a retrospective study

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ABSTRACT

Background: Main target of treatment of osteoarthritis is improvement of pain relief and functional impairment. Intra-articular triamcinolone injections are most common treatment approach in India in the non-operative management of painful osteoarthritic knee. Corticosteroids can significantly reduce local inflammatory reactions but have side effects like cartilage toxicity and increase risk of local infection. Nonsteroidal anti-inflammatory drugs have been considered as an alternative in intra-articular injections for analgesia. They have strong anti-inflammatory effects and fewer adverse reactions as compared with triamcinolone injections. The primary aim of this study was to compare the outcome of patients with symptomatic knee osteo-arthritis receiving either an intra-articular ketorolac or corticosteroid injection.

Methods: Our study is case-control, retrospective comparative study, a total of 50 patients with symptomatic knee osteoarthritis, All patients received 4, weekly injection, triamcinolone or ketorolac for first three weeks and on 4th week only intra-articular sodium hyaluronate injections. All the parameters (VAS, WOMAC) were evaluated and recorded at 1st, 2nd, 5th weeks and 3 months after first injection.

Results: At the first week, the VAS score was lower in group A, but no significant differences were found at any other time point as per WOMAC score and VAS score. And there was insignificant difference in group 1 and 2 scores.

Conclusions: Both intra-articular injections regimen showed nearly same efficacy with clinically insignificant difference, ketorolac intra-articular injection can alleviate steroid’s side effects.

Keywords: Osteoarthritis knee, Intra-articular steroid, Intra-articular ketorolac, Intra-articular hyaluronic acid

INTRODUCTION

Pain is most common symptom in knee osteoarthritis and can lead to functional impairment for patients. Main target of treatment of osteoarthritis is improvement of pain relief and functional impairment. There are many treatment modalities such as physiotherapy, medical, and surgical approaches.1 Intra-articular triamcinolone injections are most common treatment approach in India in the nonoperative management of painful osteoarthritis knee. Corticosteroids can significantly reduce local inflammatory reactions. However, their increased use can have negative implications such as cartilage toxicity and increase risk of local infection, which results in damage of articular cartilage elasticity.2 The main factor contributing to the symptoms and disability in osteoarthritis is ongoing inflammatory reaction. Nonsteroidal anti-inflammatory drugs have been considered as an alternative in intra-articular injections for analgesia.3 They have strong anti-inflammatory effects and fewer adverse reactions as compared with triamcinolone injections. Ketorolac (NSAIDS) causes
platelet dysfunction and gastrointestinal toxicity, but local application may supply higher tissue concentrations with fewer systemic complications. There are very less researches available regarding intra-articular ketorolac injections for symptomatic knee osteo-arthritis. We also gave intra-articular hyaluronate for visco-supplement which known to improve cartilage health. The primary aim of this study was to compare the outcome of patients with symptomatic knee osteo-arthritis receiving either an intra-articular ketorolac or corticosteroid injection.

METHODS

Our study is case-control, retrospective comparative study. From August 2020 to November 2021, a total of 50 patients (30 females and 20 males) with symptomatic knee osteo-arthritis, age ranges from 45 to 75 years (mean age, 58.8±9.9 years), were enrolled in this retrospective study. Study is approved by university ethical committee. Study was done in department of orthopaedics, trauma centre, institute of medical sciences, Banaras Hindu University, Uttar Pradesh. All patients had taken medical or physiotherapy for at least 3 months with no or minor improvement in symptoms. Patients were randomly assigned to receive intra-articular triamcinolone or ketorolac injections. Selection criteria: osteo-arthritis with grade II-III (Kellgren and Lawrence), who signed the informed agreement form for participation). Main excluded participants for this study included a history or presence of trauma or surgery or cancer or malignant tumours, infections and sores on the target knee, history of vasovagal shock, use of NSAIDs in 2 days prior to injection, any receiving corticosteroids injection in the knee in the last 6 months, pregnancy and lactation. Exclusion Criteria was chronic pain management, allergy to NSAIDs or steroids, prior surgery, kidney disease that would preclude NSAID administration, significant autoimmune diseases, any injection in the knee 3 months prior, and severe neurological or psychiatric diseases. Intra-articular Injection Regimen: All patients received 4 weekly injection, triamcinolone or ketorolac for first three weeks and on 4th week only intra-articular sodium hyaluronate injections by the same physician, aceclofenac (100 mg orally twice daily) and oral cefuroxime (250 mg, twice daily) was administered as for 3 days. The oral regimen was permitted after each injection, and other oral analgesics during the study period were not given. Other supportive Medications other aceclofenac (analgesic) were permitted so that patients could maintain their regular therapy. All the parameters were evaluated and recorded at 1st, 2nd, 5th weeks and 3 months after first injection. The study was double blinded during the entire research period. All the intra-articular injections were performed by the same orthopaedic surgeon with a superolateral approach: Group 1: a 10-ml of a mixed intra-articular drug regimen (5 ml of 0.5% lidocaine and 40 mg of triamcinolone and Group 2: a 10-ml intra-articular injection of a mixed drug regimen (5 ml of 0.5% lidocaine and 10 mg of ketorolac) and 2 week later each group received) 6 ml of sodium hyaluronate (48 mg). Current study documented: age, sex, body mass index, Kellgren-Lawrence grade, side of knee Osteo-arthritis, pain duration and pain visual analog scale (VAS) score, and Western Ontario and McMaster Universities Osteoarthritis Index (WOMAC) score before the injection; Pain intensity (rest/movement) was assessed using a 10-cm horizontal VAS, 21 with 0 cm indicating “no pain” and 10 cm indicating “worst pain.” Pain at rest was assessed after a 30-minute rest. The WOMAC was employed to evaluate knee function. The overall response to treatment was evaluated by the Rubin scale (1¼ poor; 2¼ fair; 3¼ good; 4¼ excellent). Successful treatment was defined as a Rubin score of good or excellent. The side effects and complications (evaluated just from a clinical examination) were also recorded.

Statistical analysis

Statistical analysis was done using SPSS (Version 17.0; IBM). Variables are presented as means with standard deviations. The characteristics of the two groups were analysed by the student t test, chi-square test, p<0.05 was considered to indicate statistical significance.

RESULTS

Out of 50 patients included in study, 25 patients were in group 1 and 25 patients in group 2. Group 1 had 16 females (64%) and 9 males (36%), mean age of 58.6±9.2 years, mean BMI of 21.76±1.62, average duration of symptoms was 10.46±3.26 months. Group 2 had 14 females (56%) and 11 males (44%), mean age of 59.5±10.16 years, mean BMI of 20.85±1.72, average duration of symptoms was 11.46±4.32 months. Patients from both group 1 and 2 had a significant improvement in their VAS and WOMAC scores from the first injection to final follow-up. At latest follow-up, no significant differences were found in the successful treatment rate between these 2 groups. Pain findings the mean VAS pain scores of both groups decreased significantly from baseline to each follow-up time point. At the first week, the VAS score was lower in group A, but no significant differences were found at any other time point. No patient lost follow-up. Patient condition was improved from initial time after injection and each follow up time in both group 1 and group 2 as per WOMAC score. And there was insignificant difference in group 1 and 2 scores.

Complications

There was only minor complication in 2 patients which was local inflammation and pain which subsided after 3 days of analgesic, ice compression and rest.

DISCUSSION

In this study, we found that osteoarthritis is more common in late 50’s and more common in females 64% and 56% in both groups respectively.
It was observed that intra-articular ketorolac injections provided the same pain relief and functional relief. Visual analog Scores Before Injection 1 weeks, 2 weeks, 5 weeks and 3 months in Group 1; 7.24±0.88, 2.46±0.73, 2.24±0.14, 2.82±0.46, 2.24±0.14 Group 2; 7.84±0.37, 3.10±0.59, 2.29±0.51, 2.42±0.18, 2.48±0.35 with p value 0.302, 0.041, 0.512, 0.305, 0.706. Data are shown as mean±standard deviation. WOMAC scores before injection 1 weeks 2 weeks 5 weeks 3 months, group 1; 48.40±3.22, 32.46±4.32, 24.58±3.76, 22.04±2.28, 22.98±3.86. Group 2; 49.13±4.26, 33.71±3.98, 26.12±4.21, 22.79±2.66, 23.38±4.10 and p value are 0.584, 0.382, 0.794, 0.344, 0.280. Data are shown as mean±standard deviation, WOMAC (Western Ontario and McMaster universities osteoarthritis index). Also, no serious complications were found in either group. These data showed that both intra-articular regimes decreased pain, improved functional outcome and mean ofVAS and WOMAC score are nearly same before injection with statistically insignificant difference and after injection scores improved in both group at follow-ups with statically insignificant differences in both group 1 and 2. Hyaluronic acid which is component of synovial fluid and cartilage has been widely accepted as a visco-supplement for the treatment of knee OA pain. It gives viscoelastic supplement that improves movement of articular joints. Huang et al conducted a randomized, double-blind, multi-centre placebo-controlled study to evaluate the efficacy and tolerability of sodium hyaluronate for the treatment of knee OA. Also, the researchers suggested that 5 weekly intra-articular injections of sodium hyaluronate are well tolerated, can provide sustained relief of pain, and improve function. Altman et al also evaluated the safety of sodium hyaluronate for painful knee OA. They found that repeat injections of sodium hyaluronate were effective, safe, well tolerated, and not associated with an increase in adverse events. It is quite possible that some of benefits seen in our patients were a result of sodium hyaluronate. While primary knee osteo-arthritis is not a classic inflammatory arthropathy, it is usually associated with inflammation. This inflammatory reaction is the main factor contributing to the symptoms of pain and the progression of osteo-arthritis. Some inflammatory cytokines such as bradykinin or histamine can directly stimulate the primary afferent nociceptive fibres, while others can decrease the pain threshold via sensitizing the primary afferent nociceptive fibres to stimulus. Additionally, synovitis is considered an early feature in OA and is not just found in advanced OA. Synovial inflammation can exacerbate cartilage destruction and pain levels because of the of inflammatory cytokines, which results in the release of degradative enzymes and modulates pain perception. Main nonoperative management of early symptomatic knee osteo-arthritis is intra-articular corticosteroid injections which can markedly reduce inflammation and relieve pain via a minimally invasive method. The anti-inflammatory mechanism of action of corticosteroid is multifactorial: in general, it inhibits antigen opsonization; cell adhesion and migration; and the synthesis and release of cytokines, leukotrienes, prostaglandins, and neutrophil superoxide. In our study, patients who received triamcinolone injections achieved successful outcomes at 5 weeks after treatment commencement and 3 months after the last injection, respectively. In a study by Hepper et al intrarticular corticosteroid injections demonstrated a statistically and clinically significant reduction in pain when compared with placebo. However, their increased use can have negative implications including chondral toxicity and a high risk of infections. Ketorolac found as a promising analgesic medication. Within the past years, it has been widely used in arthroscopic surgery and arthroplasty alone or combined with another agents. After shoulder arthroscopic surgery, adding ketorolac to intra-articular analgesia injections has been recognized as a safe and effective method to improve pain relief. In this study, intraarticular ketorolac injections demonstrated similar pain relief and functional benefits compared with intraarticular cortisone injections. Overall, no significant differences were found in the successful treatment rate between these 2 groups.
ld chondral damage, it is broadly perceived. operative pain in patients measured in our study. 

23 received sodium hyaluronate, and the benefits seen in should be determined by further studies. All patients pointed out that focal post-injection pain was self subsided with no supplemental treatment. Lee et al. found that mild histopathological changes might be safe and do less harm to local tissues. Dogan et al. found that mild histopathological changes noted microscopically just like normal saline. No obvious cartilage necrosis has been found after a ketorolac injection. The use of intra-articular ketorolac might be safe and do less harm to local tissues. Dogan et al. found that mild histopathological changes might be found in rabbit knee joints after an intra-articular morphine or ketorolac injection, but safety was confirmed when used intra-articularly. In the present study, only 3 patients developed focal post-injection pain for about 1 to 3 days. All of the pain complaints were self-limited and subsided with no supplemental treatment. Lee et al. pointed out that focal post-injection pain was associated with local ketorolac concentrations. Till the date no study present about the dose of ketorolac present and should be determined by further studies. All patients received sodium hyaluronate, and the benefits seen in both groups could be attributed to that. Ideally, we should compare only triamcinolone acetonide with ketorolac for a true comparison. The other limitations in our study. First, this was a retrospective study in design, but the extensive inclusion and exclusion criteria described controlled the shortcomings. Second, the radiographic results of cartilage degeneration were not followed up by any method in our study and our follow-up duration is also short. The short follow-up only showed the efficacy of the single treatment and avoided the influences of other however; it does not give information on the possible long-term effects of the injections. The current study shows that when combined with sodium hyaluronate, intra-articular ketorolac produced the same pain relief and functional improvement as corticosteroid at 3 months after an injection.

### CONCLUSION

Current study shows osteo-arthritis started in late 40’s and more common in females in India. Both intra-articular injections regimen showed nearly same efficacy with clinically insignificant difference, steroids have chondrototoxicity and increase risk of local infection. NSAIDs intra-articular injection can alleviate this side effect. However large sample size and long term follow up required for further evidences.

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### REFERENCES
