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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 osteoarthritis 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 osteo-arthritis, 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 inta-articular hyaluronate for visco-supplement which known to improve cartilage heath.[4] 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).[5-6] 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.[7] The overall response to treatment was evaluated by the Rubin scale (1 ¼ poor; 2 ¼ fair; 3 ¼ good; 4 ¼ 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.

Table 1: Demographic data (n=50).

Data	Group A	Group B	P value
Age(years)	58.6±9.2	59.5±10.16	0.501
Sex (female/male)	16/09	14/11	0.624
Body mass index(kg/m2)	21.76±1.62	0.85±1.72	0.184
pain duration, month	10.46±3.26	11.59±4.32	0.625
Side (left/right)	12/13	11/14	0.539
Kellgren-Lawrence (grade 2/3)	15/10	14/11	0.526
VAS pain score	7.64±0.82	7.65±0.60	0.310
WOMAC score	48.60±4.29	7.83±4.58	0.226

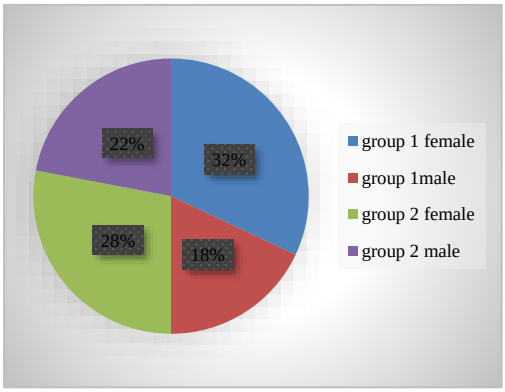

Figure 1: Distribution of sex within group 1 and group 2.

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 of VAS 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.[8] 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[4] also evaluated the safety of sodium hyaluronate for painful knee OA. They founded 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.[9]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.[10] 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.[11,12] Main nonoperative management of early symptomatic knee osteo-arthritis is intra-articular corticosteroid injections 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.[13-16] 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 intra-articular corticosteroid injections demonstrated a statistically and clinically significant reduction in pain when compared with placebo.[17] However, their increased use can have negative implications including chondral toxicity and a high risk of infections.[18] 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.[19-22] 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.

Table 2: VAS score.

Groups	Before inj.	1 week	2 weeks	5 weeks	3 months	P value
Group 1	7.24±0.88	2.46±0.73	2.24±0.14	2.82±0.46	2.24±0.14	0.513
Group 2	7.84±0.37	3.10±0.59	2.29±0.51	2.42±0.18	2.48±0.35	
P value	0.302	0.410	0.512	0.305	0.706	

Table 3: WOMAC score (mean±SD).

Groups	Before inj.	1 week	2 weeks	5 weeks	3 months	P value
Group 1	48.40±3.22	32.46±4.32	24.58±3.76	22.04±2.28	22.98±3.86	0.513
Group 2	49.13±4.26	33.71±3.98	26.12±4.21	22.79±2.66	23.38±4.10	
P value	0.584	0.382	0.794	0.344	0.280	

The safety of intra-articular corticosteroid injections is still controversial. Side effects associated with intraarticular corticosteroid injections do exist. Other known complications include an increased incidence of joint infections, skin atrophy, and tendinopathy. Although cortisone injections may increase a patient's risk for an infection and chondral damage, it is broadly perceived among clinicians that complications after a joint injection are indeed rare.[2] A survey of orthopaedic surgeons was used to quantify the perceived risk of infections after a joint injection.[23] 50% surgeons perceived the risk of infections as 1 in 1000 injections, and 33% perceived the risk as even lower, at 1 in 10,000. Considering the negative potential side effects, some researchers have suggested that the frequency of steroid injections should be less than once every 3 months.A clinical trial by Raynauld et al examined the effect of 40 mg of triamcinolone acetonide in patients with OA by administering injections every 3 months for 2 years.[24] Long-term triamcinolone acetonide administration prevented narrowing of the radiographically measured joint space over a 2 year study period.[25] Based on clinical experience; we choose 3 weekly injections of intra-articular corticosteroid over the 5-week injection period to prevent possible cartilage damage. As an alternative choice, ketorolac shows some clinical safety. Intra-articular ketorolac injections have produced degenerative changes noted microscopically just like normal saline. No obvious cartilage necrosis has been found after a ketorolac injection.[26] 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.[27] 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 chondrotoxicity 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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Ethical approval: The study was approved by the Institutional Ethics Committee

REFERENCES

1. Min OW, Thae BM. Efficacy of physical modalities in knee osteoarthritis: recent recommendations. Int J Phys Med Rehabil. 2016;4:e112.
2. Wernecke C, Braun HJ, Dragoo JL. The effect of intra-articular corticosteroids on articular cartilage: a systematic review. Orthopaed J Sports Med. 2015; 3(5):23-5.
3. Xu J, Qu Y, Li H, Jiang T, Zheng C, Wang B, Shen P. Effect of ketorolac in intra-articular injection analgesia for postoperative pain in patients

undergoing shoulder arthroscopy: a pilot-controlled clinical study. Journal of pain research. 2019;12:417.
4. Altman RD, Rosen JE, Bloch DA, et al. Safety and efficacy of retreatment with a bioengineered hyaluronate for painful osteoarthritis of the Knee: results of the open-label extension study of the flexxtrial. Osteoarthritis cartilage. 2011;19(10):1169-75.
5. Kellgrenjh L. Radiological assessment of osteoarthrosis. Ann Rheum Dis. 1957;16(4):494-502.
6. Kohn MD, Sassoon AA, Fernando ND. Classifications in brief: Kellgren-Lawrence classification of osteoarthritis. Clin Orthopaed Related Res. 2016;474(8):1886-93.
7. Bellamy N, Buchananw W, Goldsmith CH, Campbell J, Stittl W. Validation study of womac: a health status instrument for measuring Clinically important patient relevant outcomes to antirheumatic drug Therapy in patients with osteoarthritis of the hip or knee. J rheumatol.1988;15:1833-40.
8. Huang TL, Chang CC, Lee CH. Intra-articular injections of Sodium hyaluronate (hyalgan®) in osteoarthritis of the knee: a randomized, controlled, double-blind, multicenter trial in the asian population. BMC Musculoskelet Disord. 2011;12:221.
9. Bonnet CS, Walsh DA. Osteoarthritis, angiogenesis and inflammation. Rheumatol (Oxford). 2005;44:7-16.
10. Dray A. Inflammatory mediators of pain. Br J Anaest. 1995;75(2):125-31.
11. Creamer p. Intra-articular corticosteroid injections in osteoarthritis: do They work and if so, how? Ann Rheum Dis. 1997;56:634-6.
12. Desai A, Ramankutty S, Board T, Raut V. Does intraarticular steroid Infiltration increase the rate of infection in subsequent total knee Replacements? Knee. 2009;16:262-4.
13. Dogan N, Erdema F, Gundogdu C, Kursad H, Kizilkaya M. The effects of ketorolac and morphine on articular cartilage and synovium in the Rabbit knee joint. Can J Physiolpharmacol. 2004,82:502-5.
14. Farooq MA, Devitt AT. Perceived efficacy and risks of infection following intra-articular injections: a survey of orthopaedic surgeons. Irj Med Sci. 2005; 174:26-32.
15. Freire V, Bureau V. Injectable corticosteroids: take precautions and use caution. Semin Musculoskelet Radiol. 2016;20(5):401-8.
16. Kontinneny T, Kemppinen P, Segerberg M, Hukkanen M, Rees R, Santavirta S. Peripheral and spinal neural mechanisms in arthritis with Particular reference to treatment of inflammation and pain. Arthritis Rheum. 1994;37:965-82.
17. Hepper CT, Halvorson JJ, Duncanst T et al. The efficacy and duration Of intraarticular corticosteroid injection for knee osteoarthritis: a systematic review of level 1 studies. J Am Acadorthop Surg. 2009;17: 638-46.
18. Mcgarryj G, Daruwallaz J. The efficacy, accuracy and complications Of corticosteroid injections of the knee joint. Knee Surg Sports Traumatolarthrosc. 2011; 19(10):1649-54.
19. Li J, li Q. Expert consensus on the application of sodium hyaluronate In the treatment of osteoarthritis. 2012 ed. Chinese J Med Front. 2012:4(11):1-8.
20. Rubin D. Cervical radiculitis: diagnosis and treatment. Arch Phys Med Rehab. 1960;41:580-6.
21. Reuben SS, Connelly NR. Postoperative analgesia for outpatient Arthroscopic knee sugery with intraarticular bupivacaine and ketorolac. Anesthanalg. 1995;80:1154-7.
22. Shapiro PS, Rohder S, Froimson MI, Lash RH, Postak P, Greenwald AS. The effect of local corticosteroid or ketorolac exposure on histologic and biomechanical properties of rabbit tendon and cartilage. Hand. 2007;2:165-72.
23. Raynauld JP, Buckland-Wright C, Ward R. Safety and efficacy of Long-term intraarticular steroid injections in osteoarthritis of the knee: a randomized, double-blind, placebo-controlled trial. Arthritis Rheum. 2003;48:370-7.
24. Spector TD, Hart DJ, Andra D. Low-level increases in serum c-reactive protein are present in early osteoarthritis of the knee and predict progressive disease. Arthritis Rheum. 1997;40:723-7.
25. Tehranzadeh J, Booya F, Root J. Cartilage metabolism in osteoarthritis and the influence of viscosupplementation and steroid: a review. Actaradiol. 2005;46:288-96.
26. Uthman I, Raynauld JP, Haraoui B. Intra-articular therapy in osteoarthritis. Postgrad Med J. 2003; 79(934):449-53.
27. Lee SC, Rhad W, Chang WH. Rapid analgesic onset of intraarticular Hyaluronic acid with ketorolac in osteoarthritis of the knee. J back Musculoskelet Rehab. 2011;24(1):31-8.

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