

**Role of Intra-Articular Hyaluronic Acid Injection in the Management of Early Osteoarthritis of Knee Joint**Nilesh Kothari<sup>1</sup>, Priyank Deepak<sup>2</sup>, Sandeep Chouhan<sup>3</sup>, Rajesh Chouhan<sup>4\*</sup>, Tushar Ghodawat<sup>5</sup><sup>1</sup>MS Orthopaedics, Junior Consultant, Department of Center for Bone and Joints, BCM Kokilaben Dhirubhai Ambani Hospital, Indore, Madhya Pradesh, India<sup>2</sup>DNB Orthopaedics, Surgery, Senior Resident, Department of Orthopaedics, Nalanda Medical College and Hospital, Agam Kuaan, Patna<sup>3</sup>DNB Orthopaedics, Junior Consultant, Department of Center for Bone and Joints, Kokilaben Dhirubhai Ambani Hospital, Indore, Madhya Pradesh, India<sup>4</sup>MS Orthopaedics, Senior Resident, Department of Orthopaedics, RD Gardi Medical College, Ujjain, Madhya Pradesh, India<sup>5</sup>MS Orthopaedics, Assistant Professor, Department of Orthopaedics, LNCT Medical College and Sewakunj Hospital, Indore, Madhya Pradesh, India

Received: 11-01-2024 / Revised: 12-02-2024 / Accepted: 15-03-2024

Corresponding Author: Dr Rajesh Chouhan

Conflict of interest: Nil

**Abstract****Background:** Knee osteoarthritis (OA) is a common entity in adults causing disability and decreased work productivity. Management of early OA is not established showing varied results of conservative and medical treatment.**Aims and Objectives:** We evaluated the functional outcome of intra-articular injection of hyaluronic acid (HA) in OA knee or the management of early stages of OA knee.**Material and Methods:** 50 patients of OA knee, Kellgren type II or III, more than 45 years of age, were treated with 6 ml of intra-articular HA injection and were assessed by improvement in functional outcome as seen by WOMAC and VAS score.**Results:** The mean age was  $52.65 \pm 6.4$  years (range 45 to 70 years). 19 (38%) were males and 31 (62%) were females. 17 (34%) patients had KL grade 2 and 33 (66%) patients had KL grade 3 osteoarthritis. The mean pre-procedural WOMAC score of  $46.7 \pm 6.4$  improved to  $22.73 \pm 5.78$ ,  $22.6 \pm 5.02$  and  $24.83 \pm 5.59$  at 4 weeks, 12 weeks, and 24 weeks after the HA injection, respectively. The mean pre-procedural VAS score of  $5.16 \pm 0.82$ , improved to  $1.22 \pm 1.01$ ,  $1.19 \pm 0.60$ , and  $1.52 \pm 0.55$  at 4 weeks, 12 weeks, and 24 weeks after the HA injection, respectively. Pain at the injection site was seen in 2 (4%) patients and 1 (2%) patient developed superficial infection.**Conclusion:** HA injection provides pain relief and improves the functional outcome in the early stages of Osteoarthritis of Knee.**Keywords:** Osteoarthritis, WOMAC score, hyaluronic acid, VAS score.This is an Open Access article that uses a funding model which does not charge readers or their institutions for access and distributed under the terms of the Creative Commons Attribution License (<http://creativecommons.org/licenses/by/4.0>) and the Budapest Open Access Initiative (<http://www.budapestopenaccessinitiative.org/read>), which permit unrestricted use, distribution, and reproduction in any medium, provided original work is properly credited.**Introduction**

Knee osteoarthritis occurs in 11% of people over 60 years old. A chronic degenerative disease, osteoarthritis (OA) causes a progressive loss of joint cartilage with local inflammation and periarticular bone reconstruction. [1] In addition to causing pain, stiffness, swelling, and a decrease in joint range of motion, cartilage lesions significantly affect quality of life. OA, however, is caused and developed by multiple risk factors affecting the whole joint, including cartilage, subchondral bone, synovium, ligaments, and menisci. [2] Joint replacement is a well-established treatment for severe arthritis.

However, various conservative and medical modalities have not resulted in satisfactory results in the early stages of osteoarthritis. Currently, treatment is focused on reducing symptoms and slowing the progression of the disease. Non-pharmacological treatments include patient education and self-management, exercises, weight reduction, walking supports (crutches), bracing, shoe and insole modification, local cooling/heating, acupuncture, and electromagnetic therapy. [3,4] Pharmacological treatments include topical and oral NSAID, [5] intra-articular (IA) injections of corticosteroids,

Visco supplements, and blood-derived products, including platelet-rich-plasma (PRP) (highly recommended when the use of oral analgesics or anti-inflammatories fails to release disease symptoms). [6,7] OA pain can be relieved temporarily with intra-articular (IA) corticosteroids when used in conjunction with core treatment. This approach, however, has limited efficacy in delaying disease progression, as well as undesirable potential side effects when administered at high doses and frequency. [8,9] In this context, HA is proposed as a potential treatment capable of improving the clinical condition of patients with osteoarthritis. A limited number of publications on HA, this study was designed to the efficacy of a single intra-articular dose of HA for the treatment of early OA knee. Intra articular hyaluronic acid injection is an able alternative treatment for early OA knee compared to pharmacotherapy and physiotherapy. The extracellular matrix of cartilage and synovial fluid both include hyaluronic acid, which gives them their viscoelasticity and lubricating qualities. [10] The addition of exogenous HA, or its derivatives, by intra-articular injection, addresses the degradation of hyaluronic acid in the synovial fluid of patients with knee osteoarthritis [11] and helps to restore the elastic and viscous properties of the synovial fluid, leading to pain relief and functional improvement. Additionally, HA inhibits chondrocyte death, interacts with mediators of inflammation and matrix turnover in joint cells, and has a biosynthetic chondroprotective impact. [12] The objective of this study is to evaluate the clinical benefits of HA when injected into the intra-articular space, which is a recognized pharmacological treatment in patients with mild to moderate symptomatic knee OA. We hypothesized that intra-articular injection of HA reduces pain and better functional recovery at a 6-month follow-up.

### Materials and Method

This study was conducted on 50 arthritic knees treated with HA therapy, and presented to the Department of Center for Bone and Joints at our institute from January 2023 to February 2024. Before the study written well-informed consent was obtained from all the patients. All patients of Kellgren (KL) type II or III osteoarthritis knee with more than 45 years of age were included in the study. Patients with less than 45 years, Kellgren type IV OA knee, OA with significant joint deformity, inflammatory arthritis, patellofemoral arthritis, or associated with systemic disorders such as rheumatoid arthritis or infection were excluded from the study.

A thorough history and comprehensive clinical examination of the patients was done and details were recorded in the customized proforma designed for the study. Weight-bearing standing AP and lateral view X-rays of the affected knee were taken.

Pre- Pre-procedural WOMAC knee score and VAS score were calculated.

### Procedures

After selecting those patients fulfilling the inclusion criteria, a weight-bearing x-ray of both knee joints in two planes (anteroposterior and lateral) will be taken and graded using the KELLGREN-LAWRENCE (K-L) radiographic atlas. Patients have been given 6ml of intraarticular hyaluronic acid injection (10mg/ml) via the Anterolateral approach under strict aseptic precaution, Pt in a supine position, parts painted and draped with the knee flexed to 60°, lateral joint line is palpated easily and needle is inserted laterally of the patellar tendon, [13] with the needle pointing towards the femoral notch. [14] This method only goes through Hoffa's fat pad, bypassing major blood vessels and the extensor apparatus. After inserting the needle, SF or any effusion was aspirated, 1ml of lignocaine was given, followed by 6ml of intraarticular hyaluronic acid injection given by preloaded sterile syringe, Passive mobilization of the knee was done for even distribution of the drug, the patient was observed for 30 min for any allergic reaction. After the procedure, all patients were sent home and the patients were prescribed ice fomentation, antibiotics, and paracetamol orally for 3 days. Range of motion exercise, light aerobic activities, and strength training exercises were started as per the patient's tolerance. Patients were followed regularly at 4 weeks, 12 weeks, and 24 weeks and were reassessed for functional outcomes by WOMAC knee score and VAS score. Statistical analysis was performed using the SPSS program for statistical analysis, version 12.0 for Windows, and statistical significance was set at  $p < 0.05$ .

### Results

50 patients of OA knee with a mean age of  $52.65 \pm 6.4$  years (range 45 to 70 years) were included in the study. 19 (38%) were males and 31 (62%) were females. 21 (42 %) patients had left-side involvement and 29 (58 %) patients had right side was affected. 17 (34%) patients had KL grade 2 and 33 (66%) patients had KL grade 3 osteoarthritis. 43 (86%) patients had no co-morbidities. 4 (8%) patients had associated hypertension and 3 (6%) patients had diabetes mellitus.

The mean pre-procedural WOMAC score of  $46.7 \pm 6.4$  improved to  $22.73 \pm 5.78$ ,  $22.6$

$\pm 5.02$  and  $24.83 \pm 5.59$  at 4 weeks, 12 weeks, and 24 weeks after the HA injection, respectively (table 1). The mean pre-procedural VAS score of  $5.16 \pm 0.82$ , improved to  $1.22 \pm 1.01$ ,  $1.19$ .

$\pm 0.60$  and  $1.52 \pm 0.55$  at 4 weeks, 12 weeks, and 24 weeks after the HA injection, respectively (table 1). Pain at the injection site was seen in 2 (4%) patients and 1 (2 %) patient developed a superficial

infection at the site of injection which healed with complications. antibiotics. In 47(94 %) patients there were no

#### WOMAC SCORE after HA Injection

Duration	[Mean±SD]	't' Value	P value
Pre-operative	46.7± 6.4	14.784	0.001*
At 4 weeks	22.73 ± 5.78	Df = 29	
At 4 weeks	22.73 ± 5.78	0.348	0.713
At 12 weeks	22.6 ± 5.02	Df = 29	NS
At 12 weeks	22.6 ± 5.02	-3.748	0.001*
At a 6 month	24.83 ± 5.59	Df = 29	

#### VAS SCORE after HA Injection

Duration	[Mean±SD]	't' Value	P value
Pre operative	5.16 ± 0.82	15.931	0.001*
At 4 weeks	1.22 ± 1.01	Df = 29	
At 4 weeks	1.22 ± 1.01	0.000	1.000
At 12 weeks	1.19 ± 0.60	Df = 29	NS
At 12 weeks	1.19 ± 0.60	-3.445	0.001*
At a 6 month	1.52 ± 0.55	Df = 29	

#### Discussion

Knee Osteoarthritis (OA) is one of the most common problems in aging adults, causing pain, disability, and morbidity, which had been treated conservatively by oral chondroprotective, intra-articular injections of steroids, or viscosupplements. [1,2]

Earlier OA was considered initially a degenerative disorder and a natural occurrence of "wear-and-tear" on joints as a result of aging leading to mechanical and biological events that destabilize the normal processes of degradation and synthesis of articular cartilage chondrocytes, extracellular matrix, and subchondral bone leading to increased water content, decreased proteoglycan content and altered collagen matrix, finally causing degeneration of articular cartilage. [15] Recent research evidence is changing and it is suggested that impaired remodeling and repair of damaged tissue is the main cause and so if we could prevent this, it may be possible to arrest the progress and even reverse the changes. [16]

We evaluated the role of intra-articular injection of HA for the management of 50 early stages of OA knee patients in terms of improvement in functional score and found that the mean WOMAC score of  $46.7 \pm 6.4$  pre-procedural improved to  $24.83 \pm 5.59$  and mean VAS score of  $5.16 \pm 0.82$  pre-procedural, improved to  $1.52 \pm 0.55$  at 24 weeks after the HA injection, respectively. Various studies have demonstrated the efficacy and advantageous effect of HA in OA knee.

Moreland LW et al [17] study Exogenous HA enhances chondrocyte HA and proteoglycan synthesis, reduces the production and activity of proinflammatory mediators and matrix metalloproteinases,

and alters the behavior of immune cells. Many of the physiological effects of exogenous HA may be a function of its molecular weight. Several physiological effects probably contribute to the mechanisms by which HA exerts its clinical effects on knee OA.

Antonio Gigante et al [18] studied In knee OA, viscosupplementation with 3-5 weekly intra-articular HA injections diminishes pain and improves disability, generally within 1 week and for up to 3-6 months, and is well tolerated. HA viscosupplementation is a valuable treatment approach for OA patients if other therapies are contraindicated or have failed.

V Legré-Boyer et al [19] studied Viscosupplementation has demonstrated moderate but significant efficacy (20%) versus placebo in terms of pain and function, with a high rate of responders (60-70%) in knee osteoarthritis. It allows reduced administration of opioid analgesics and NSAIDs, with an improved risk/benefit ratio and may delay joint replacement.

Kirk A Campbell et al [20] suggests that IA-HA is a viable option for knee OA. Its use results in improvements in knee pain and function that can persist for up to 26 weeks. IA-HA has a good safety profile, and its use should be considered in patients with early knee OA.

Monique P Curran [21] Clinical scores of pain/inflammation and visual analogue scale (VAS) scores of pain during walking improved from baseline values for up to 6 months after treatment with HA

Our results were similar to these studies although we haven't compared it with any other alternative treatment method.

Thus intra-articular HA injection is a safe, effective, and feasible treatment option for the management of early osteoarthritis knee. It is minimally invasive and without the risk of immunological reaction. It demonstrates clinical improvement in self-reported pain and functional capacity with no major side effects. Despite these proven efficacies, there are some issues related to HA administration that need to be sorted out by further studies like, ideal preparation, dosage, frequency and duration of HA, and the population.

### Conclusion

The use of HA injection in the treatment of osteoarthritis knee has high efficacy and safety, being a simple, economical, and short procedure, which requires less surgical skill and can be done in OPD/Minor procedure without any major complications.

### References

1. Wright EA, Katz JN, Cisternas MG, Kessler CL, Wagenseller A, Losina E. Impact of knee osteoarthritis on health care resource utilization in a US population-based national sample. *Med Care*. 2010;48(9):785–91.
2. Dhillon MS, Patel S, John R. PRP in OA knee – update, current confusions and future options. *SICOT J* 2017; 3:27:1-6.
3. Bland JH. The reversibility of osteoarthritis: a review. *Am J Med*. 1983;74(6A):16-26.
4. Michael JW, Schlüter-Brust. KU, Eysel P. The epidemiology, etiology, diagnosis, and treatment of osteoarthritis of the knee. *Dtsch Arztebl Int* 2010; 107:152-62.
5. Steinmeyer J, Bock F, Stove J, Jerosch I, Flechtenmacher J. Pharmacological treatment of knee osteoarthritis: special considerations of the new German guideline. *Orthop Rev (Pavia)*. 2018. 10(4):7782.
6. Lee KS, editor. Platelet-rich plasma injection. *Seminars in musculoskeletal radiology*. New York: Thieme Medical Publishers; 2013.
7. Boswell SG, Cole BJ, Sundman EA, et al. Platelet-rich plasma: a milieu of bioactive factors. *Arthroscopy* 2012;28(3):429–39.
8. Ostergaard M, Halberg P. Intra-articular corticosteroids in arthritic disease: a guide to treatment. *BioDrugs* 1998; 9:95-103.
9. Creamer P. Intra-articular corticosteroid treatment in osteoarthritis. *Curr Opin Rheumatol* 1999; 11:417-21.
10. Lawrence RC, Helmick CG, Arnett FC, Deyo RA, Felson D'T, Giannini EH et al. Estimates of the prevalence of arthritis and selected musculoskeletal disorders in the United States. *Arthritis Rheum*. 1998; 41:778-99.
11. Padda AS, Mohan V, Singh J, Deepti SS, Singh G, Dhillon HS. Health profile of the aged persons in urban and rural field practice areas of Medical College, Amritsar. *Indian J of Com Med*. 1998; 23:72-6.
12. Franssen M, Bridgett L, March L, Hoy D, Penserga E, Brooks P. The epidemiology of osteoarthritis in Asia. *Int J Rheum Dis*. 2011; 14(2):113-21.
13. Bijsterbosch J, Wassenaar MJE, le Cessie S, Slagboom PE, Rosendaal FR, and Huizinga TWI et al. Doyle Index is a valuable additional pain measure in osteoarthritis, *Osteoarthritis and Cartilage*, 2010;18:8.
14. Temple Michele, Ren Shuwen, Quach Phu, Hansen Bradley, Chen C. Albert & Hasegawa, Akihiko & D. DL ima, Darryl & Koziol, Jim & Masuda, Koichi & Lotz, Martin & Sah, Robert. Hyaluronan concentration and size distribution in human knee synovial fluid: Variations with age and cartilage degeneration. *Arthritis Research & Therapy*; c2016.p. 18. 10.1186/s13075-016-0161-6.
15. Rutjes AW, Jüni P, da Costa BR, Trelle S, Nüesch E, Reichenbach Viscosupplementation for osteoarthritis of the knee: a systematic review and meta-analysis. *Ann Intern Med* 2012;157:180-91.
16. Bellamy NI, Campbell J, Robinson V, Gee T, Bourne R, Wells G. Visco-supplementation for the treatment of osteoarthritis of the knee. *Cochrane Database Syst Rev*.2006;2:CD005321.
17. Moreland LW. Intra-articular hyaluronan (hyaluronic acid and hylans for the treatment of osteoarthritis: mechanisms of action. *Arthritis Research & Therapy*.2003;5(2):54-67.
18. Antonio Gigante, Leonardo Callegari. The role of intra-articular hyaluronan (Sinovial) in the treatment of osteoarthritis, Epub 2010 Nov 28.
19. V Legré-Boyer. Viscosupplementation: techniques, indications, results Epub 2015 Jan 14.
20. Kirk A Campbell 1, Brandon J Erickson 2, Bryan M Saltzman 2, Randy Mascarenhas 3, Bernard R Bach Jr 2, Brian J Cole 2, Nikhil N Verma 2 Is Local Viscosupplementation Injection Clinically Superior to Other The rapiesin the Treatment of Osteoarthritis of the Knee: A Systematic Review of Overlapping Meta-analyses, 2015 Oct;31(10):2036-45.e14.
21. Monique P Curran. Hyaluronic acid (Supartz®): a review of its use in osteoarthritis of the knee. 2010 Nov 1;27(11):925-41.