

# Efficacy of Hyaluronic Acid in Patients with Osteoarthritis of The Knee

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## Abstract

Osteoarthritis (OA) of the knee is the most common chronic degenerative joint disease characterized by pain, stiffness, swelling and progressive functional limitation in elderly. Non-surgical management modalities like physical therapy, lifestyle modification and oral non-steroidal anti-inflammatory drugs, are often ineffective or do not alleviate symptoms adequately. Intra-articular corticosteroid (CS) and hyaluronic acid (HA) injections have been used for long to alleviate the symptoms of knee OA. viscosupplementation has been used as a therapeutic modality for the management of knee OA. The principle of viscosupplementation is based on the physiological properties of the hyaluronic acid (HA) in the synovial joint which helps tissue lubricate, cushion and reduce pain in the joint.

Study diagnosed forty patient of knee Osteoarthritis for both gender with age (45-70 years) and observed change and effectiveness to pre-and post of HA injection, All patients diagnosed by Orthopedists and Rheumatologists whose used X-rays were graded as stage I, II and III according to Kellgren and Lawrence scale.

All the measurements were used at the time of enrollment in the study before any injection and then measured again at the end of three months by using Western Ontario and McMaster University Osteoarthritis Index (WOMAC) .

All the patients before therapy were having minimum score of 72.4 & 9.045 for Mean and Standard Deviation respectively while after the therapy there score reduced to 36.2 & 4.783.

The results show improvement significant during four month under study and the effect peaks at around 8–12 weeks following administration, This supports the potential use of intra-articular HA as an effective long therapeutic option for patients with OA of the knee.

**Keywords:** Osteoarthritis, hyaluronic acid , hyaluronate physiochemical functions, extracellular matrix, glycosaminoglycan , Knee Intra-articular injection.

## Introduction

Osteoarthritis of the knee is the most common slowly progressive chronic degenerative joint disease, characterized by varying degrees of loss of joint cartilage with local inflammation, usually affecting the elderly population<sup>1</sup> . There is cartilage damage combined with

a significant reduction in the viscoelastic properties of the synovial fluid and the molecular weight and concentration of the naturally occurring hyaluronic acid in synovial fluid decreases<sup>2</sup> . This loss of viscoelasticity decreases the lubrication between joint surfaces and erodes the articular surfaces and is the mechanism of origin of pain in osteoarthritis<sup>3</sup> . The patient presents with pain, swelling, stiffness, deformity, decreased range of motion and disability, which significantly affect the quality of life. The knee is the most common joint that is affected in the population with OA and plays an important role in weight bearing and mobility<sup>4</sup> .

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Treatment is aimed at reducing symptoms like reducing pain and inflammation and maintaining performance and normal movement of the joints and slowing the progression of the disease <sup>5</sup>. It includes holistic therapeutic modalities including non-pharmacological measures like patient education, physical therapy with exercises to maintain range of motion and strength, lifestyle modifications such as dieting and weight reduction <sup>6</sup>. The aim of this study was to assess the efficacy of HA intra-articular injections in managing osteoarthritic knee pain.

### Characteristics of Hyaluronic Acid (HA)

HA is a glycosaminoglycan constituent of synovial fluid and cartilage matrix in normal joints. The properties of the synovial fluid are dependent on the concentration of HA and its molecular weight (MW); in OA, the concentration and MW of HA are decreased <sup>7</sup>. The exogenous HA available for IA viscosupplementation is formulated as different MW preparations: low (range: 500,000–730,000Da), intermediate (800,000–2,000,000Da), and high MW (average: 6,000,000Da) including cross-linked formulations of HA <sup>8</sup>.

Its physiological properties include shock absorption, traumatic energy dissipation, protective coating of the articular cartilage surface and lubrication. In vitro, it is shown to have anti-inflammatory effects on cells, <sup>5,6</sup> and it may slow chondrocyte apoptosis in OA by binding CD44 and ICAM-1 receptors, and regulating in this way the process of cartilage matrix degradation. The concentration and the molecular weight of HA in the synovial fluid of patients with knee OA are shown to be reduced <sup>9</sup>.

### Study population

A total of 40 subjects were enrolled in this study in accordance to various criteria. These included gender (15 man and 25 woman), age (45-70 years) and Grade of disease by Kellgren-Lawrence (K-L) severity grade I, II and III OA of the knee <sup>10</sup>. All subjects collected from different cities and diagnosed by specialist doctors.

### Materials and Methods

This prospective randomized study was diagnosed 40 patients (53 knees) with knee osteoarthritis who were treated with a single intra-articular injection of HA by

88mg/4ml lightly cross-linking HA (Monovisc®, Anika Therapeutics, Inc).

All patients who were diagnosed with knee OA by Orthopedists and Rheumatologists who used X-rays were graded as stage I, II and III according to Kellgren and Lawrence scale <sup>11</sup>. The injection was given at a site near the superolateral pole of patella in the suprapatellar pouch under aseptic conditions, with knee kept in 15-20 degree flexion and the patient was advised to take 1 day of rest after injection and apply ice to the area if there were any signs of inflammation.

All the measurements were used at the time of enrollment in the study before any injection and then measured again at the end of 3 months by using Western Ontario and McMaster University Osteoarthritis Index (WOMAC) was used as a self-administered test to compare as regards pain and functional improvement pre and post used the HA injection, with the use of WOMAC (Appendix 1), a lower score represented a better outcome <sup>12</sup>.

### WOMAC

The WOMAC is a self-administered questionnaire that is composed of 24 questions categorized into three subscales (pain, stiffness, and physical function). In the current study, we used 5-point Likert scale format: none (0), mild (1), moderate (2), severe (3), and extreme (4). Scores for each subscale were determined by summing the component item scores for each subscale—possible score range: pain (0–20), stiffness (0–8), and physical function (0–68). The final total scores (possible score range, 0–96) were determined by summing the scores for each subscale <sup>13,14</sup>. WOMAC-total score in the range of 0 (best score) to 96 (worst score).

### Results

Forty patients enrolled in our study suffered from osteoarthritis, who were treated with HA

intra-articular injections. Pain and stiffness and physical function on knee patients were estimated pre and post treatment by used WOMAC index.

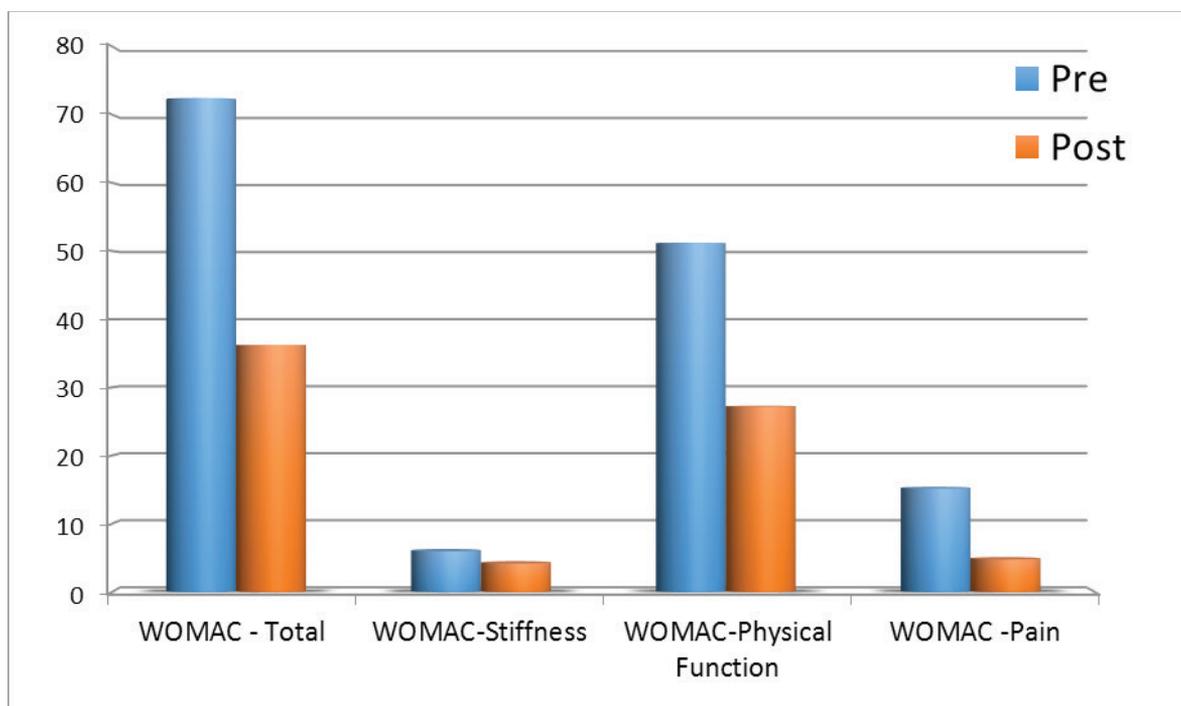
The subjective scoring with WOMAC score done after 4 months showed gradual decrease in WOMAC score which suggests that the patients have observed

relief in pain, stiffness and physical has improved due to importance of hyaluronic acid (HA) and its physiological and biochemical functions at cellular level (Table 1) . All the patients before therapy were having minimum score of 72.4 & 9.045 for Mean and Standard Deviation respectively while Significant improvement ( $p < 0.05$ ) were obtained After the therapy there score reduced to 36.2 & 4.783 (Figure1).

And based on individual results for each patient, it was observed that best effectiveness of the HA intra-articular injections was for patients suffering from primary knee OA with Kellgren and Lawrence (KL) Grade I and II , while in patients suffering advanced OA in last grade III of Kellgren-Lawrence , it was observed that were less effective.

Statistical Analysis	Pre Therapy		Post Therapy	
	Mean	SD	Mean	SD
Pain	15.2	2.315	4.8	1.720
Physical Functioning	51.2	5.635	27.2	2.315
Stiffness	6	1.095	4.2	0.748
Total WOMAC Score	72.4	9.045	36.2	4.783

**Table 1. WOMAC Index Pre and Post treatment.**



**Figure 1. Comparison of Mean WOMAC values in Study Group Pre and Post treatment by HA injection.**

## Discussion

Primary treatment goals in knee OA include pain reduction and improvement of joint mobility and function. The secondary goal is to decrease the progression of disease. Viscosupplementation with hyaluronic acid is a non-operative intervention.

WOMAC Scores showed improvement in all the parameters post-intervention after 4 months, there is due to it keeps the space between your bones well lubricated and viscoelasticity of the synovial fluid. When the joints are lubricated, the bones are less likely to grind against each other and cause reduce pain.

Moreover hyaluronic acid supplements are very helpful for people suffering from osteoarthritis, a type of degenerative joint disease caused by wear and tear on the joints over time. whereas high-impact movements that generate compressive forces on a healthy joint benefit from the shock absorption properties of HA. Furthermore, with inflammation, HA may offer protective properties to the joint tissue by scavenging free radicals and reducing oxidative damage.

Injected HA's main functions stem from its antinociceptive properties, ability to improve the viscoelastic properties of synovial fluid, and indirect lubrication of the joint through stimulated endogenous HA synthesis. Other potential anecdotal benefits of HA injections that have been proposed include chondroprotection and potential function as a disease-modifying agent for OA. More specifically, Type II collagen degradation products appear to be a marker of cartilage degradation and OA disease activity.<sup>15</sup>

The improvement was more significant in Hyaluronic acid at the end of 4 months providing a good cue to compare the clinical efficacy before and after intervention over four months

## Conclusion

According to results, the intra-articular HA injection was very effective in pain relief and improvement of knee function beginning from three months.

There is good evidence for the efficacy of HA injection in reducing pain and increasing function in knee OA. this supports the potential use of intra-articular

HA as an effective long therapeutic option for patients with OA of the knee and we recommends that use of HA injectoin in knee OA patients with mild to moderate disease to get best result.

**Conflict of Interests:** Nil.

**Ethical Clearance:** Take from AL-Hussein Teaching Hospital by approval ethical committee.

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