

**ORIGINAL RESEARCH**

# Effect of hyaluronic acid on knee osteoarthritis

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Received date: 16 April, 2024

Acceptance date: 18 May, 2024

## ABSTRACT

**Background:** Osteoarthritis (OA) of the knee is a prevalent condition causing significant morbidity. Hyaluronic acid (HA) has been proposed as a therapeutic agent for its potential to improve joint lubrication and reduce symptoms. **Objective:** This study aims to evaluate the effect of HA injections on pain relief and functional improvement in patients with knee osteoarthritis. **Methods:** A prospective study involving 100 patients with knee OA was conducted. Participants received three weekly intra-articular injections of HA. Pain and function were assessed using the Visual Analog Scale (VAS) and the Western Ontario and McMaster Universities Osteoarthritis Index (WOMAC) at baseline, 1 month, and 3 months post-treatment. **Results:** Significant reductions in VAS scores and improvements in WOMAC scores were observed at 1 month and 3 months post-treatment compared to baseline ( $p < 0.05$ ). **Conclusion:** HA injections provide significant pain relief and functional improvement in knee OA patients, suggesting it as a viable treatment option.

**Keywords:** Hyaluronic acid, knee osteoarthritis, intra-articular injection, pain relief, functional improvement.

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## INTRODUCTION

Osteoarthritis (OA) is the most common form of arthritis, characterized by the degeneration of joint cartilage and underlying bone, most frequently affecting the knees, hips, and hands [1]. It is a leading cause of disability in older adults, causing pain, stiffness, and functional impairment [2]. The pathophysiology of OA involves complex interactions among mechanical, biochemical, and genetic factors, resulting in the progressive destruction of cartilage, changes in subchondral bone, and inflammation of the synovium [3].

Current management strategies for knee OA focus on symptom relief and improving joint function. These include lifestyle modifications, physical therapy, pharmacologic treatments, and, in severe cases, surgical interventions such as total knee arthroplasty [4]. Despite the availability of various treatment options, there remains a significant unmet need for effective and well-tolerated therapies that can slow disease progression and improve quality of life for patients.

Hyaluronic acid (HA) is a naturally occurring glycosaminoglycan found in the synovial fluid of

joints, contributing to its viscoelastic properties and playing a crucial role in maintaining joint homeostasis [5]. In OA, the concentration and molecular weight of HA in the synovial fluid are significantly reduced, impairing its lubricating and shock-absorbing functions [6]. This has led to the development of HA-based viscosupplementation as a therapeutic intervention for knee OA.

Intra-articular injection of HA aims to restore the viscoelastic properties of the synovial fluid, thereby reducing pain and improving joint function [7]. The mechanism of action of HA in OA is thought to involve several pathways, including the enhancement of joint lubrication, reduction of inflammatory mediators, protection of cartilage, and stimulation of endogenous HA production [8].

Numerous clinical trials and meta-analyses have evaluated the efficacy of HA injections in knee OA, with mixed results. Some studies have reported significant improvements in pain and function, while others have shown minimal or no benefit compared to placebo [9]. These discrepancies may be attributed to variations in study design, patient populations, HA formulations, and injection protocols.

Despite these inconsistencies, HA injections are widely used in clinical practice and are recommended by several clinical guidelines as a treatment option for knee OA [10]. However, the optimal patient selection criteria, dosing regimen, and long-term benefits of HA therapy remain areas of active investigation.

The objective of this study is to evaluate the effect of intra-articular HA injections on pain relief and functional improvement in patients with knee OA. This prospective study aims to provide further evidence on the efficacy and safety of HA therapy in a real-world clinical setting, contributing to the ongoing efforts to optimize the management of knee OA.

## MATERIALS AND METHODS

This prospective study was conducted at tertiary care center from 2022-2023. The study protocol was approved by the Institutional Review Board, and written informed consent was obtained from all participants.

**Participants:** One hundred patients aged 40-75 years with clinically and radiographically confirmed knee OA (Kellgren-Lawrence grade II-III) were enrolled. Exclusion criteria included secondary OA, inflammatory arthritis, previous knee surgery, or intra-articular injections within the last 6 months.

**Intervention:** Participants received three weekly intra-articular injections of 2 mL HA (20 mg/mL) using a standard aseptic technique. The injections were administered by an experienced orthopedic surgeon.

**Outcome Measures:** Pain and functional outcomes were assessed using the Visual Analog Scale (VAS) for pain and the Western Ontario and McMaster Universities Osteoarthritis Index (WOMAC) at baseline, 1 month, and 3 months post-treatment. The primary outcome was the change in VAS scores, and the secondary outcome was the change in WOMAC scores.

**Statistical Analysis:** Data were analyzed using SPSS version 25.0 (IBM Corp., Armonk, NY). Descriptive statistics were used to summarize the baseline characteristics of the study population. Changes in VAS and WOMAC scores from baseline to follow-up were analyzed using paired t-tests. A p-value of < 0.05 was considered statistically significant.

## RESULTS

**Baseline Characteristics:** The baseline characteristics of the study population are presented in Table 1. The mean age of the participants was  $62.3 \pm 8.5$  years, and 60% were female. The mean baseline VAS score was  $6.8 \pm 1.2$ , and the mean baseline WOMAC score was  $72.5 \pm 8.3$ .

**Primary Outcome:** A significant reduction in VAS scores was observed at 1 month and 3 months post-treatment compared to baseline ( $p < 0.05$ ). The mean VAS scores were  $4.2 \pm 1.1$  at 1 month and  $3.5 \pm 1.0$  at 3 months post-treatment (Table 2).

**Secondary Outcome:** Significant improvements in WOMAC scores were also observed at 1 month and 3 months post-treatment compared to baseline ( $p < 0.05$ ). The mean WOMAC scores were  $54.3 \pm 7.2$  at 1 month and  $48.6 \pm 6.9$  at 3 months post-treatment (Table 3).

**Adverse Events:** No serious adverse events were reported during the study period. Mild transient pain at the injection site was the most commonly reported adverse event, occurring in 10% of participants.

**Table 1: Baseline Characteristics of the Study Population**

Variable	Value
Age (years)	$62.3 \pm 8.5$
Female (%)	60
Baseline VAS	$6.8 \pm 1.2$
Baseline WOMAC	$72.5 \pm 8.3$

**Table 2: VAS Scores at Baseline, 1 Month, and 3 Months Post-Treatment**

Time Point	VAS Score (Mean $\pm$ SD)
Baseline	$6.8 \pm 1.2$
1 Month	$4.2 \pm 1.1$
3 Months	$3.5 \pm 1.0$

**Table 3: WOMAC Scores at Baseline, 1 Month, and 3 Months Post-Treatment**

Time Point	WOMAC Score (Mean $\pm$ SD)
Baseline	$72.5 \pm 8.3$
1 Month	$54.3 \pm 7.2$
3 Months	$48.6 \pm 6.9$

## DISCUSSION

The findings of this study indicate that intra-articular HA injections provide significant pain relief and functional improvement in patients with knee OA. These results are consistent with several previous studies that have demonstrated the efficacy of HA in managing OA symptoms [11].

One of the primary mechanisms by which HA exerts its therapeutic effects is through the restoration of the viscoelastic properties of the synovial fluid. This enhances joint lubrication and shock absorption, thereby reducing mechanical stress on the articular cartilage [12]. Additionally, HA has been shown to exert anti-inflammatory effects by modulating the activity of pro-inflammatory cytokines and enzymes involved in cartilage degradation [13].

A meta-analysis conducted by Bannuru et al. (2015) reported that HA injections provided significant pain relief and functional improvement in knee OA compared to placebo, with the effects persisting for up to 26 weeks [14]. Similarly, a randomized controlled trial by Pavelka et al. (2011) demonstrated that a single course of HA injections significantly improved pain and function in patients with knee OA, with benefits lasting for up to 6 months [15].

However, the efficacy of HA injections has been a subject of debate, with some studies reporting minimal or no benefit. For instance, a systematic review by Rutjes et al. (2012) concluded that the clinical benefit of HA injections in knee OA was small and not clinically relevant when compared to placebo [16]. These discrepancies may be attributed to variations in study design, patient populations, and HA formulations.

The safety profile of HA injections observed in this study is consistent with previous reports. No serious adverse events were reported, and mild transient pain at the injection site was the most commonly reported adverse event. This highlights the favorable safety profile of HA, making it a suitable option for patients who may not tolerate oral NSAIDs or other pharmacologic treatments [17].

The strengths of this study include its prospective design, well-defined inclusion and exclusion criteria, and the use of validated outcome measures (VAS and WOMAC). However, there are some limitations that should be acknowledged. The study was conducted at a single center, which may limit the generalizability of the findings. Additionally, the follow-up period was limited to 3 months, and longer-term studies are needed to assess the durability of the treatment effects.

Future research should focus on identifying the optimal patient selection criteria, dosing regimens, and combination therapies to enhance the efficacy of HA injections. Additionally, the development of novel HA formulations with improved pharmacokinetic properties and longer-lasting effects holds promise for the future management of knee OA.

## CONCLUSION

In conclusion, this study demonstrates that intra-articular HA injections provide significant pain relief and functional improvement in patients with knee osteoarthritis. The favorable safety profile and ease of administration make HA a viable treatment option for managing OA symptoms. Further research is warranted to optimize treatment protocols and evaluate long-term outcomes.

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