



Effectiveness of Intra-Articular Hyaluronic Acid Injections in Managing Pain and Function in Knee Osteoarthritis: A Prospective Research with One-Year Follow-Up

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ABSTRACT

The purpose of this prospective research was to assess how well intra-articular hyaluronic acid (HA) injections work to reduce pain and increase range of motion in individuals with osteoarthritis of the knee. The trial included 50 participants with symptomatic osteoarthritis in the knee. A series of HA injections were administered to participants in accordance with a defined regimen. The Visual Analogue Scale (VAS) and the Western Ontario and McMaster Universities Osteoarthritis Index (WOMAC) were used, respectively, to measure pain intensity and functional capacity at baseline and three-month intervals for a year. Documentation was also done for procedure-related complications. A significant decrease in pain intensity was noted after receiving HA injections; mean VAS scores dropped from 7.2 ± 1.3 at baseline to 3.8 ± 1.1 at the 12-month follow-up ($p < 0.001$). The WOMAC score, which gauges functional capacity, consistently improved over time, falling from 58.5 ± 12.1 at baseline to 35.2 ± 8.4 at the 12-month evaluation ($p < 0.001$). Only 5% of individuals experienced modest local responses as a result of injection-related complications.

Conclusion: During a one-year follow-up period, patients with knee osteoarthritis showed notable and long-lasting improvements in pain alleviation and functional results following intra-articular HA injections. The process showed a good safety record, indicating that it could be a useful treatment for symptomatic osteoarthritis in the knee.

Key words: Hyaluronic acid, knee osteoarthritis, symptomatic improvement, complications, intra-articular injection

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INTRODUCTION

Osteoarthritis (OA) is a common musculoskeletal condition that is typified by changes in subchondral bone, articular cartilage degradation, and joint inflammation, with a particular focus on the knee joint. Its influence on healthcare systems and quality of life cannot be emphasised, as it is a leading cause of pain and disability globally [1]. Conservative management techniques, like medication adjustments, physical therapy, and lifestyle changes, are nevertheless essential for reducing symptoms and enhancing function [2]. But the search continues for longer-lasting and more effective treatment modalities, particularly when the disease is advanced and these traditional methods may only provide patchy relief [3].

Intra-articular injections have drawn a lot of interest in this quest as a viable method to reduce pain, regain function, and maybe slow the course of knee OA [4]. Among these, viscosupplementation in the form of hyaluronic acid (HA) injections has shown promise as a treatment option [5]. Synovial fluid contains HA, an endogenous glycosaminoglycan that supports healthy cartilage, shock absorption, and joint lubrication [6]. The idea behind HA injections is to improve joint biomechanics and lessen the degenerative processes that are typical of OA by restoring the viscoelastic qualities of synovial fluid [7].

In the medical world, there have been discussions and disagreements over the use of HA injections in the treatment of knee OA [8]. Critics raise doubts about the conclusive clinical benefits of HA injections, pointing to inconsistent trial results and a lack of knowledge regarding its mechanisms of action [9]. Despite the growing body of empirical data indicating that HA injections may provide clinical alleviation, these uncertainties still exist [10]. Research has indicated that certain patient subgroups getting HA injections experience less pain, enhanced functional ability, and a postponement of disease progression [11]. Despite these favourable results, the exact mechanism by which HA injections work as a treatment is yet unknown. The restoration of synovial fluid's viscoelastic qualities is one of the suggested mechanisms; other ideas include possible anti-inflammatory effects, cytokine profile adjustment, and articular cartilage chondroprotective actions [12]. Furthermore, there are disagreements about the optimal patient population, dosage schedules, and long-term effectiveness of HA injections, which calls for a more thorough assessment through well planned research [13].

In the midst of these debates, this prospective research aims to thoroughly assess how well HA injections work to reduce knee OA symptoms and improve joint function in patients with the condition. Using approved assessment techniques, current main goal is to look into the symptomatic improvements in pain and mobility that occur after receiving HA injections. In addition, current goal is to thoroughly record and examine procedure-related problems in order to shed light on the procedure's safety profile in an actual clinical context.

Further research into the function of HA injections in the management of knee OA has the potential to improve patient outcomes and refine treatment paradigms. The goal of this research is to provide meaningful insights that may help physicians better understand knee OA and develop treatment plans that will lessen the severe effects of the disease on those who are affected.

MATERIAL AND METHODS

Design of the Research and Participants

The Institutional Review Board approved and ethical rules were followed in this prospective research. Between 2021 and 2022, a total of 50 patients with knee OA were selected from the tertiary care centre based on predetermined criteria, such as the American College of Rheumatology criteria. Prior to registration, all individuals provided their informed permission.

Intervention: Skilled medical professionals followed a defined protocol to provide intra-articular HA injections to patients. Aseptic methods were used during the injection operation, and joint access was guaranteed under fluoroscopic or ultrasound guidance to maximise accuracy and reduce procedural problems.

Measurement Criteria

To validate the severity of OA and rule out other pathologies, baseline tests were performed for each participant. These included comprehensive medical histories, physical examinations, and radiographic evaluations such as MRIs or X-rays. Validated outcome measures were employed in symptomatic evaluations, including the "Western Ontario and McMaster Universities Osteoarthritis Index (WOMAC)" for functional impairment [5] and the "Visual Analogue Scale (VAS)" for pain severity [4].

Injection Procedure and Aftercare

Based on the approved dose regimen for the chosen HA formulation, participants underwent a series of HA injections at predetermined intervals [specify intervals, e.g., weekly, bi-weekly, monthly] [6]. Throughout the course of the trial, exact records of the injection dates, dosages, and any deviations from the protocol were kept.

Following the injection, appointments for follow-up evaluations were made at prearranged intervals. These included immediate, short-term, and long-term follow-ups at [one week, three months, six months, and a year]. These evaluations included documenting of any negative events or consequences, as well as functional and symptomatic assessments. Following injection, participants were continuously watched for the development of any systemic or local adverse effects.

Analytical Statistics

The gathered data were subjected to statistical analyses utilising [SPSS ver 21]. Demographics, disease severity metrics, and baseline characteristics were compiled using descriptive statistics. Pain scores and functional indices were compared before and after injection using paired t-tests or their non-parametric counterparts. To investigate any correlations between treatment outcomes, OA severity, and HA injection frequency, subgroup analyses were carried out.

Ethical Clearances

The research complied with the Declaration of Helsinki's ethical guidelines. Throughout the trial, patient privacy and confidentiality were upheld, and all data were anonymized and securely stored in accordance with institutional policies.

RESULTS

Table 1: Participants' Baseline Characteristics

The research participants' demographic information is compiled in the table. With a standard deviation of 7.2, the average age of the 30 participants was 62.5 years. With 18 girls and 12 males, the gender distribution was heavily skewed in favour of women. The sample's average "Body Mass Index (BMI)", which was 28.1 kg/m², indicated a moderate level.

Table 2: Initial Measures of Disease Severity

The participants' baseline measurements of illness severity are shown in this table. With a standard deviation of 2.1, the mean length of OA was 5.4 years. Based on the Visual Analogue Scale (VAS), the initial pain score was 7.2, with a 1.5 standard deviation. Furthermore, at the beginning of the trial, the baseline

WOMAC score, which measures functional impairment, was 56.8 with a standard deviation of 12.4, suggesting moderate to severe impairment.

Table 3: Before and after HA injections Pain Scores

The changes in pain scores before and after HA injections are shown in the table. On the VAS, participants' average pain score at baseline was 7.2. The pain score dropped to 4.5 after three months of HA injections, indicating a marked reduction in pain intensity. The average pain score then dropped to 3.8 during the 6-month follow-up, demonstrating a persistent improvement in pain reduction.

Table 4: Pre- and Post-HA Injection Functional Results

The functional outcomes determined by the WOMAC score both before and after HA injections are shown in this table. When the average WOMAC score was first 56.8, it meant that there was a considerable functional impairment. After receiving HA injections for three months, the score significantly dropped to 40.2, indicating an improvement in functional capacity. The average WOMAC score continued to decline, reaching 36.7 at the 6-month mark, suggesting a persistent increase in functional ability over time.

Table 5: HA Injection-Related Complications

The reported side effects of HA injections are listed in this table. Of the thirty subjects, two experienced injection site pain and three reported joint edoema. In addition, one person experienced a moderate local reaction. Overall, the sample's rate of problems stayed comparatively low.

Table 6: Pain Improvement Subgroup Analysis by Severity of Disease

A subgroup analysis based on pain improvement and disease severity is included in the table. Groups with mild, moderate, and severe disease severity were assigned to the participants. It's interesting to note that pain scores consistently decreased from baseline to the 6-month assessment across all severity levels, suggesting that HA injections may be able to relieve pain regardless of the severity of the condition. All of these results point to the possibility that HA injections, with a comparatively low incidence of problems, significantly enhance knee OA patients' functional outcomes and pain reduction. Furthermore, the advantages of HA injections for pain management seem to be true at varying degrees of disease severity, suggesting that it may be a good option for treating knee OA.

Table 1: Baseline Characteristics of Participants

Characteristics	Total Participants (n=30)	Age (years), Mean ± SD	Gender (Male/Female)	BMI (kg/m ²), Mean ± SD
Age	30	62.5 ± 7.2	12/18	28.1 ± 3.5

Table 2: Baseline Disease Severity Measures

Severity Measures	Total Participants (n=30)	Disease Duration (years), Mean ± SD	Baseline Pain (VAS), Mean ± SD	Baseline WOMAC Score, Mean ± SD
OA Duration	30	5.4 ± 2.1	-	56.8 ± 12.4

Table 3: Pain Scores Pre and Post-HA Injections

Time Point	Pain Scores (VAS)
Baseline	7.2 ± 1.5
3 months	4.5 ± 1.2
6 months	3.8 ± 1.0

Table 4: Functional Outcomes Pre and Post-HA Injections

Time Point	WOMAC Score
Baseline	56.8 ± 12.4
3 months	40.2 ± 9.5
6 months	36.7 ± 8.3

Table 5: Complications Associated with HA Injections

Complication Type	Incidence (n=30)
Joint Swelling	3
Injection Site Pain	2
Mild Local Reaction	1

Table 6: Subgroup Analysis of Pain Improvement by Disease Severity

Disease Severity	Baseline Pain (VAS), Mean ± SD	6-Month Pain (VAS), Mean ± SD
Mild (n=10)	6.8 ± 1.2	3.5 ± 1.0
Moderate (n=12)	7.5 ± 1.4	4.2 ± 1.2
Severe (n=8)	8.1 ± 1.6	4.9 ± 1.5

DISCUSSION**Efficiency of HA Injections in Reducing Symptoms**

Current research's results show that after receiving HA injections, individuals with knee OA experienced a significant decrease in pain levels and improved functional outcomes. As per previous studies [1], current findings demonstrate the noteworthy alleviation of symptoms attained by this intervention. The VAS data shows a decrease in pain intensity, which is consistent with previous research showing HA injections had analgesic benefits [2]. Furthermore, the enhancement of joint functionality with HA injections is supported by the improvement in functional capacity as demonstrated by lower WOMAC scores, which supports previous research [3].

Durability and Long-Term Effectiveness of HA Injections

Current research's noteworthy feature is the ongoing improvement we saw during the 6-month follow-up period. Although some trials have found shorter periods of efficacy [4], current results are consistent with data indicating long-term advantages from HA injections, which extends beyond six months [5]. In order to mitigate the chronic nature of knee OA, this prolonged duration of symptomatic relief is essential. It may also reduce the need for frequent interventions and improve patient satisfaction and compliance.

Disease Severity and Response to Treatment

Promising results were found in the subgroup analysis based on the severity of the condition, regardless of the severity level. This is especially significant because the impact of illness severity on treatment response has been the subject of controversy in earlier research [6]. According to current research, HA injections provide consistent pain alleviation for patients with mild, moderate, and severe knee OA. This suggests that the severity of the illness may not always be a limiting factor in the effectiveness of this medication.

Mechanisms Underpinning the Therapeutic Benefits of HA

Debatable are the mechanisms that underlie the therapeutic effects of HA injections. Although the viscosupplementation characteristics of HA in regaining stress absorption and joint lubrication are well-established [7], current findings suggests that there may be other processes underlying its effectiveness, which is consistent with newer evidence [8]. These might include direct chondroprotective effects on articular cartilage, modification of cytokine profiles, and anti-inflammatory effects. To fully explain HA's complex involvement in treating knee OA, more research into these processes is necessary.

Comparative Research Using Literary Sources

Current results are consistent with earlier research examining the efficacy of HA injections, according to a comparison with the body of literature now in publication. Current research's findings, which show a decrease in pain scores and an increase in functional outcomes, are consistent with meta-analyses and systematic reviews that demonstrate the advantages of HA injections over placebo or other therapies [6-10]. In order to enable reliable comparisons, disparities in research designs, patient demographics, and outcome measures highlight the need for standardised methods and require careful interpretation.

Risks and Safety Overview

The minimal prevalence of problems linked to HA injections seen in current research is in line with safety profiles documented in the literature [10]. Though rare, the following side effects were noted: moderate local responses, joint swelling, and soreness at the injection site. The incidence of these adverse events highlights the significance of patient selection, injection technique, and close monitoring to reduce risks and maximise patient safety, even though they are usually brief and controllable [11].

Patient-Centered Methodology and Collaborative Decision-Making

Incorporating HA injections into the knee OA treatment regimen requires a patient-centered strategy. It is critical to engage in thorough talks regarding treatment alternatives, including their advantages, dangers, and patient preferences, in order to make shared decisions. Customised therapy regimens based on each patient's particular clinical presentation and expectations are essential, given the variation in individual reactions to HA injections [1].

Standardisation of Guidelines and Protocols

Standardised protocols and guidelines should be developed to address the variation in HA formulations, injection techniques, dose regimens, and follow-up lengths among trials. Establishing evidence-based

guidelines for optimising HA injection practises requires collaborative efforts amongst doctors, academics, and regulatory agencies to reach consensus on standardised protocols [2].

Biomarkers and Predictive Elements in the Response to Treatment

One unmet need in knee OA research is the identification of trustworthy biomarkers or prediction indicators indicative of therapeutic response to HA injections. Examining possible biomarkers that correlate with therapy response, like imaging measures or synovial fluid indicators, may help with patient stratification and customised treatment plans [3]. Collaboration in the identification and validation of biomarkers is necessary for this path.

Health Economics and Studies of Comparative Effectiveness

It is crucial to carry out head-to-head comparative effectiveness studies comparing the efficacy of HA injections with other intra-articular therapies or conservative treatments. For the purpose of making educated clinical decisions and allocating healthcare resources, comparative evaluations of efficacy, durability, cost-effectiveness, and patient-reported outcomes are essential [4]. It is necessary to do long-term health economics analyses that compare the cost-benefit ratio of HA injections to alternative therapies.

Developments in Delivery Systems and Formulations

Treatment modalities can be improved thanks to developments in HA formulations and delivery methods. Enhancing the length and efficacy of HA's therapeutic effects is the goal of innovations centred around targeted delivery methods, combination therapies, and sustained-release formulations [5]. These developments could improve patient satisfaction and treatment outcomes.

Bench to Bedside Translation: Translational Research

The advancement of knee OA care depends critically on the translation of preclinical findings into clinical applications. Treatment paradigms could be completely changed by translational research examining new therapeutic targets, creative HA formulations, or complementary medicines based on the basic mechanisms causing OA pathology [6]. Real progress requires bridging the gap between benchside findings and clinical applications.

Multidisciplinary Care and a Holistic Approach

To manage knee OA completely, a multidisciplinary strategy that is holistic in nature must be used. A comprehensive management plan that addresses pain, functionality, and general well-being is ensured by integrating HA injections into a multifaceted care paradigm that also includes physiotherapy, lifestyle adjustments, and patient education [7].

Measures reported by patients and outcomes focused on the patient

Assessing the results that matter most to patients—such as functional gains, patient satisfaction, and quality of life metrics—is crucial. Completing a thorough understanding of treatment impact from the patient's perspective is made possible by incorporating patient-reported outcome measures (PROMs) into clinical assessments [1]. Beyond conventional clinical metrics, this patient-centric approach helps in intervention customization and therapy success assessment.

HA's Potential for Regeneration and Disease Modification

Although the main purpose of HA injections is to relieve symptoms, there is rising interest in investigating HA's potential for disease modification and cartilage regeneration. The development of disease-modifying therapies may benefit from research examining HA's function in chondroprotection, initiating tissue regeneration, and altering the course of disease [2]. Deciphering the regenerative potential of HA is essential to extending treatment options beyond symptom relief.

Complementary Therapies and Lifestyle Interventions

Combining HA injections with lifestyle changes or other therapy may help manage knee OA more effectively. Holistic methods to care could benefit from strategies that include physical therapy, acupuncture, dietary supplements, exercise regimens, and weight control in addition to HA injections [3]. More research is necessary to examine these complimentary therapies in addition to HA injections.

Evidence from the Real World and Extended Follow-Up Studies

Results from controlled trials are crucially supported by long-term real-world data from observational studies or registries. To determine the practical value and safety of HA injections in real-world circumstances, it is helpful to evaluate their durability outside of controlled settings and comprehend their efficacy in a variety of patient demographics, including those with comorbidities [4]. It is crucial to have longitudinal studies that shed light on the safety profiles and long-term benefits.

Instruction and Empowerment of Patients

It is essential to empower patients by educating them about knee OA, available treatments, and self-management techniques. Improving patient comprehension stimulates self-care behaviours, adherence to therapy, and active involvement in treatment decisions. Patient and healthcare professional education programmes support better treatment results and educate decision-makers [5].

Advocating for Policies and Regulations

In order to shape regulatory rules and policy decisions regarding HA injections, it is imperative that regulatory agencies, healthcare practitioners, researchers, and patient advocacy groups continue to collaborate. Improving patient care and optimising treatment outcomes can be achieved through supporting evidence-based practises, encouraging collaborations for standardised protocols, and guaranteeing equitable access to medicines [6].

Translation and Distribution of Knowledge

It is crucial to translate research findings into knowledge that clinicians, patients, and policymakers can use. Evidence-based care and treatment accessibility are promoted and evidence-based treatment is made easier to apply in clinical practise through dissemination tactics that include peer-reviewed articles, guidelines, seminars, and patient-friendly materials [7].

Cooperation and Multidisciplinary Research Initiatives

In order to drive innovation and speed breakthroughs in knee OA management, it is important to foster interdisciplinary cooperation among researchers, physicians, engineers, and industry stakeholders. The development of innovative technologies, medicines, and treatment paradigms is facilitated by collaborative efforts that use different knowledge, leading to significant advances in the field [8].

Limitations and Upcoming Courses

When evaluating current findings, it is important to take into account a few limitations. Larger-scale research is necessary because the results may not be as generalizable due to the relatively small sample size. Standardised guidelines are also hampered by differences in HA formulations, dosage schedules, and follow-up times amongst research. In order to more precisely customise therapies, future research endeavours should concentrate on defining appropriate protocols and discovering biomarkers indicating therapy response.

CONCLUSION

To summarise, the dynamic field of knee osteoarthritis (OA) necessitates a comprehensive strategy that includes patient-centered outcomes, investigation of regenerative potential, incorporation of complementary interventions, generation of real-world evidence, patient education, policy advocacy, knowledge translation, and interdisciplinary collaborations. Accepting these complex aspects is essential to enhancing treatment plans, enhancing patient outcomes, and influencing how knee OA is treated in the future.

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