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Original Research Article

Role and Effectiveness of Intra-Articular Injection of Hyaluronic Acid in the Treatment of Knee Osteoarthritis: A Prospective Study

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Abstract:

Background: Intra-articular injection of hyaluronic acid (IAHA) is a widely utilized therapeutic approach for knee osteoarthritis, although its efficacy remains a topic of debate.

Aim and Objective: This prospective study aimed to evaluate the effectiveness and safety of IAHA therapy in patients with knee osteoarthritis.

Materials and Methods: Thirty patients with knee osteoarthritis were treated with three IAHA injections over one year. Pain severity was assessed using the Visual Analog Scale (VAS), while knee function was evaluated using the Western Ontario and McMaster Universities Osteoarthritis Index (WOMAC). A radiographic evaluation was performed to monitor disease progression. Adverse events were documented throughout the study period. Subgroup analyses were conducted based on demographic and clinical characteristics.

Results: Following IAHA therapy, a significant reduction in knee pain severity was observed, with the mean VAS score decreasing from 7.2 ± 1.5 at baseline to 3.4 ± 1.2 at six months post-treatment ($p < 0.001$). Similarly, knee function improved significantly, as evidenced by a decrease in the mean WOMAC score from 45.6 ± 9.8 to 22.3 ± 6.7 ($p < 0.001$). Radiographic evaluation revealed no significant disease progression. Transient local reactions at the injection site were reported in 16.7% of patients, but no serious adverse events were documented. Subgroup analyses did not identify significant variations in treatment response based on age, gender, disease severity, or comorbidity profiles.

Conclusion: Intra-articular injection of hyaluronic acid effectively reduced pain and improved knee function in patients with knee osteoarthritis, with a favorable safety profile and no evidence of disease progression on radiographic evaluation. These findings support the continued use of IAHA therapy as a viable treatment option for knee osteoarthritis.

Keywords: Knee Osteoarthritis, Intra-Articular Injection, Hyaluronic Acid, Pain Relief, Functional Improvement.

Introduction

Osteoarthritis (OA) is one of the most prevalent musculoskeletal disorders globally, characterized by progressive degeneration of articular cartilage, synovial inflammation, and joint pain, particularly affecting weight-bearing joints such as the knee. [1] Among the myriad of therapeutic modalities available, intra-articular injection of hyaluronic acid (IAHA) has emerged as a promising intervention for managing knee osteoarthritis, offering symptomatic relief and potentially modifying the disease process. [2]

The rationale behind IAHA administration is rooted in the physiological role of hyaluronic acid (HA) within the synovial fluid, where it contributes to joint lubrication, shock absorption, and overall joint homeostasis. [3] In osteoarthritic joints, endogenous HA's concentration and molecular weight are often diminished, leading to impaired lubrication and increased susceptibility to mechanical stress, inflammation, and cartilage degradation. [4] By supplementing exogenous HA via intra-articular injection, it is hypothesized that the viscoelastic properties of the synovial fluid can be restored, thereby alleviating pain, improving joint function, and potentially slowing down the progression of knee osteoarthritis. [5]

Despite the widespread use of IAHA in clinical practice, controversies persist regarding its

efficacy, optimal dosing regimens, patient selection criteria, and long-term outcomes. [6] While some studies have reported significant symptomatic improvements and disease-modifying effects following IAHA therapy, others have yielded conflicting results or failed to demonstrate superiority over alternative interventions such as corticosteroid injections or placebo. [7]

In this prospective study, we aim to comprehensively evaluate the role and effectiveness of IAHA in treating knee osteoarthritis, with a focus on elucidating its clinical outcomes, safety profile, and potential mechanisms of action. By employing rigorous methodology, including standardized outcome measures, validated assessment tools, and longitudinal follow-up, we endeavor to provide robust evidence to inform clinical decision-making and optimize patient care.

Through meticulous analysis of patient-reported outcomes, functional assessments, radiographic findings, and biochemical markers, we seek to elucidate the impact of IAHA on pain relief, physical function, joint structure, inflammatory biomarkers, and quality of life in individuals with knee osteoarthritis. Furthermore, by exploring potential predictors of treatment response and identifying subgroups of patients who may derive maximal benefit from IAHA therapy, we aspire to tailor treatment strategies and enhance therapeutic outcomes in this challenging population.

Materials and Methods

Study Design: This prospective study was conducted at TSM Medical College, Lucknow, over a one-year period. The Institutional Ethics Committee approved the study protocol, and written informed consent was obtained from all participants before enrollment.

Participants: A total of 30 patients diagnosed with knee osteoarthritis, according to the American College of Rheumatology criteria, were recruited from the outpatient department of TSM Medical College. Inclusion criteria comprised individuals aged 40 years or older, with clinical and radiographic evidence of knee osteoarthritis (Kellgren-Lawrence grade II-III) and moderate to severe knee pain (Visual Analog Scale score ≥ 40 mm). Patients with a history of previous knee surgery, intra-articular injections within the past three months, inflammatory joint disease, infection, contraindications to hyaluronic acid therapy, or inability to provide informed consent were excluded from the study.

Intervention: All enrolled patients received three intra-articular hyaluronic acid injections (IAHA) weekly. The HA formulation used in this study was administered according to the manufacturer's instructions. The injections were administered under aseptic conditions by experienced physicians, using standardized techniques for knee joint access.

Outcome Measures: The primary outcome measure was the change in knee pain severity from baseline to follow-up assessments, as measured by the Visual Analog Scale (VAS) score. Secondary outcome measures included improvements in knee function, which were assessed using the Western Ontario and McMaster Universities Osteoarthritis Index (WOMAC) and patient-reported global assessment of disease activity. Additionally, radiographic evaluation of joint structure was performed using weight-bearing anteroposterior knee radiographs at baseline and six months post-treatment. The study systematically monitored and documented adverse events and complications associated with IAHA therapy.

Statistical Analysis: Depending on the data distribution, statistical analysis was performed using appropriate parametric or non-parametric tests. Descriptive statistics were used to summarize demographic and clinical characteristics of the study population. Paired t-tests or Wilcoxon signed-rank tests were employed to assess changes in outcome measures from baseline to follow-up. Subgroup analyses and multivariate regression modeling were conducted to explore potential predictors of treatment response and factors influencing clinical outcomes.

Ethical Considerations: The study used principles outlined in the Declaration of Helsinki and Good Clinical Practice guidelines. Patient data confidentiality was strictly maintained, and participants were assured of their right to withdraw from the study at any time without prejudice.

Results

Demographic and Clinical Characteristics: Thirty patients participated in the study, 18 of whom were male (60.0%) and 12 female (40.0%). The mean age of the participants was 58.4 years (SD ± 7.2). Table 1 details baseline demographic and clinical characteristics.

Table 1: Baseline Demographic and Clinical Characteristics of Study Population

Characteristic	Mean ± SD / N (%)
Age (years)	58.4 ± 7.2
Gender	
Male	18 (60.0)
Female	12 (40.0)

Body Mass Index (BMI)	28.3 ± 3.5
Duration of OA (years)	6.7 ± 2.1
Kellgren-Lawrence Grade	
II	12 (40.0)
III	18 (60.0)
Comorbidities	
Hypertension	10 (33.3)
Diabetes Mellitus	8 (26.7)
Others	12 (40.0)
Baseline VAS score	7.2 ± 1.5
Baseline WOMAC score	45.6 ± 9.8

Primary Outcome: Following three intra-articular injections of hyaluronic acid, a statistically significant reduction in knee pain severity was observed compared to baseline. The mean VAS score decreased from 7.2 ± 1.5 at baseline to 3.4 ± 1.2 at six months post-treatment ($p < 0.001$).

Secondary Outcomes: Improvements in knee function, assessed by the WOMAC, were observed post-treatment. The mean WOMAC score decreased from 45.6 ± 9.8 at baseline to 22.3 ± 6.7 six months post-treatment ($p < 0.001$).

Radiographic Evaluation: A radiographic assessment conducted at a follow-up of six months revealed no significant progression of joint space narrowing or osteophyte formation in the treated knee joints. The mean joint space width remained relatively stable, with no statistically significant changes observed compared to baseline measurements.

Adverse Events: No serious adverse events or complications attributable to IAHA therapy were reported throughout the study period. However, 5 patients (16.7%) documented transient local reactions such as pain, swelling, or erythema at the injection site. These reactions were mild and resolved spontaneously within a few days without intervention.

Subgroup Analysis: Subgroup analyses were performed to explore potential differences in treatment response based on various demographic and clinical factors. No significant variations in treatment outcomes were observed across different age groups ($p = 0.742$), genders ($p = 0.611$), baseline disease severities ($p = 0.895$), or comorbidity profiles ($p = 0.521$). The efficacy of IAHA therapy remained consistent across all subgroups, indicating its broad applicability and effectiveness in managing knee osteoarthritis.

Discussion

In this prospective study, we investigated the role and effectiveness of IAHA in treating OA. The findings revealed significant improvements in pain relief and knee function following IAHA therapy, with a favorable safety profile and no evidence of disease progression on radiographic evaluation. These results contribute to the growing evidence supporting using IAHA as a viable therapeutic option for knee OA management.

Our study demonstrated a statistically significant reduction in knee pain severity, as measured by the VAS, from baseline to six months post-treatment. This finding is consistent with previous research indicating the analgesic properties of IAHA, attributed to its ability to restore viscoelastic properties of the synovial fluid, thereby reducing friction and mechanical stress within the joint. [8] The observed improvement in knee function, as assessed by the WOMAC, further underscores the clinical efficacy of IAHA in enhancing functional outcomes and quality of life for patients with knee OA. [9]

Radiographic evaluation at six months follow-up revealed no significant progression of joint space narrowing or osteophyte formation in the treated knee joints. This suggests a potential disease-modifying effect of IAHA, although longer-term studies with larger sample sizes are warranted to validate these findings. The absence of disease progression aligns with previous studies reporting the chondroprotective effects of HA through modulation of inflammatory pathways, cartilage matrix synthesis promotion, and cartilage degradation enzymes' inhibition. [10]

Adverse events associated with IAHA therapy were minimal in our study, consistent with the safety profile reported in existing literature. [11] Transient local reactions such as pain, swelling, or erythema at the injection site were mild and self-limiting, underscoring the tolerability of IAHA treatment in clinical practice. These findings reassure clinicians and patients regarding the safety of IAHA as a therapeutic intervention for knee OA.

Subgroup analyses did not reveal significant differences in treatment response across various demographic and clinical factors, including age, gender, baseline disease severity, and comorbidity profiles. This suggests that IAHA therapy may offer consistent benefits to a broad spectrum of patients with knee OA, irrespective of individual characteristics. However, further research is needed to elucidate potential predictors of treatment

response and optimize patient selection criteria for IAHA therapy.

Limitations of our study include its single-center design, relatively small sample size, and short-term follow-up period. Future multicenter studies with larger cohorts and longer follow-up durations are warranted to confirm the durability of treatment effects and assess long-term outcomes, including disease progression and the need for additional interventions such as total knee replacement.

Conclusion

Our study provides valuable insights into the role and effectiveness of IAHA in managing knee OA. The observed improvements in pain relief, knee function, and safety profile support the integration of IAHA into clinical practice guidelines for treating knee OA. Further research is needed to elucidate the mechanisms of action, optimize treatment regimens, and identify patient subgroups that may derive maximal benefit from IAHA therapy.

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