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HYALURONIC ACID IN THE TREATMENT OF ORTHOPAEDIC INJURIES IN ATHLETES: A NARRATIVE REVIEW OF CURRENT EVIDENCE AND CLINICAL APPLICATIONS

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ABSTRACT

Introduction and Objective: Nowadays, orthopaedic injuries are a common occurrence among athletes as a result of repetitive biomechanical stress and high physical demands. With growing interest in non-surgical and regenerative approaches in sports medicine, hyaluronic acid (HA) has emerged as a promising therapeutic option. This narrative review aims to synthesize current evidence on HA's biological properties and clinical applications in athletic populations, focusing on its role in treating tendon, ligament, and joint injuries, highlighting both its benefits and limitations, and future directions.
Methods: The review is based on articles retrieved from PubMed through July 2025. Studies involving athletic populations were prioritized, with emphasis on cohort studies, randomized controlled trials, systematic reviews, and meta-analyses.
Key Findings: HA exerts multiple therapeutic effects, including the modulation of inflammation, enhancement of synovial fluid viscosity, support for chondrocytes, and promotion of tissue regeneration. Moreover, it demonstrates beneficial effects in treating a range of sports-related conditions, including tendinopathies (e.g., Achilles and patellar tendinopathies), acute ligament injuries (e.g., ankle sprains), and early joint degeneration. Nonetheless, inconsistencies in study outcomes, heterogeneity of HA products, concerns about cost-effectiveness, and limited athlete-specific trials present ongoing challenges.
Conclusion: HA represents a valuable adjunct in the non-surgical management of orthopedic injuries in athletes. While preliminary findings are promising, more high-quality, athlete-specific research is needed to confirm its long-term efficacy, optimize treatment protocols, and explore its full potential as both a therapeutic and preventive strategy in sports medicine.

KEYWORDS

Hyaluronic Acid, Viscosupplementation, Athletes, Orthopaedic Injuries, Joint Pain, Sports Medicine

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1. Introduction

Athletes, whether in the professional or recreational field, frequently experience orthopedic injuries due to the significant biomechanical stress associated with intensive training and competition. Both acute and chronic injuries severely impact performance and prolong time away from sports, making effective and timely interventions crucial for maintaining athletic longevity and overall functionality. In most cases these injuries affect tendons, ligaments, joints and articular cartilage. In this context, non-surgical strategies that promote tissue healing, reduce inflammation, alleviate pain, and restore joint balance are particularly valuable. One of them is application of hyaluronic acid (HA).

HA, a high-molecular-weight glycosaminoglycan, is a substance naturally occurring in synovial fluid, articular cartilage, and other extracellular matrices. It plays an important role in maintaining joint homeostasis mainly through its lubricating, viscoelastic, and shock-absorbing properties [1]. Initially approved for the management of knee osteoarthritis (OA) [2], HA has gained increasing attention in sports and musculoskeletal medicine. Its clinical applications have extended beyond the elderly population to encompass younger, physically active individuals, particularly athletes, who are prone to early degenerative joint changes, repetitive microtrauma, and overload syndromes. Intra-articular administration of HA, commonly termed *viscosupplementation*, aims to restore properties of synovial fluid, provide chondroprotection, and exert anti-inflammatory and analgesic effects within the joint microenvironment [3].

The HA is not only known in sports medicine for its symptomatic benefits, such as pain relief [4] and improved joint function [5], but also safety profile and non-invasive nature [6]. Furthermore, experimental and clinical data suggest that HA plays a crucial role in tissue regeneration and cellular signaling, making it an intriguing candidate in regenerative orthopaedics [7].

2. Objective

This narrative review aims to synthesise current evidence on biological properties and applications of HA in treating orthopaedic injuries among athletes. It will explore the underlying biological properties and mechanisms, summarize clinical applications in tendon, ligament, and joint injuries, and critically examine the limitations and future directions of HA therapy in reference to sports medicine. The goal is to provide clinicians and researchers with an updated and comprehensive overview of HA's potential role in supporting athletic recovery and performance.

3. Methodology

A literature search was conducted in the PubMed database and screened in July 2025. Search terms covered 'hyaluronic acid', 'viscosupplementation', 'athletes', 'orthopaedic injuries', 'joint pain', and 'sports medicine'. Only articles published in English were included in this review. Priority was given to human studies involving athletes, including cohort studies, randomized controlled trials, systematic reviews, and meta-analyses. In vitro studies and preclinical animal trials were referenced selectively to support mechanistic explanations of HA's biological activity.

A total of 31 relevant articles were selected and reviewed in full. These included both general foundational research on HA and sport-specific clinical studies examining the use of HA in athletic populations. Data extraction focused on patient demographics (especially athletic status), type of injury (tendinopathies, acute ligament injuries and early joint degeneration), treatment protocols (e.g., HA type, dosage, and injection technique), outcomes (including pain, function, and return to sport), safety profiles, and reported limitations. Emphasis was placed on studies that investigated the use of HA in athletes or active individuals, reflecting real-world applicability in sports medicine practice.

4. Results

Eventually, all studies were sorted into four main themes: Biological Properties of HA, Clinical Applications of HA, Limitations and Future Directions.

5. Biological Properties of HA

HA is a naturally occurring, high-molecular-weight glycosaminoglycan composed of repeating β-1,4-D-glucuronic acid and β-1,3-*N*-acetylglucosamine units [1]. Although it has a relatively simple composition, HA is known for its diverse range of molecular functions.

5.1 Lubrication, Shock Absorption and Viscoelasticity

HA is responsible for producing a viscous, gel-like substance in synovial fluid. Its unique rheological properties act as a boundary lubricant, reducing friction between articular surfaces to friction coefficients as low as ~0.001 under physiological load, effectively protecting cartilage from wear and shear-induced damage [8]. In parallel, HA provides shock absorption by dampening mechanical stress and maintaining joint stability during impact or repetitive motion; loss of its concentration in osteoarthritis correlates with increased joint trauma [9].

5.2 Chondroprotection and Cellular Signaling

Moreover, HA supports cartilage integrity through both mechanical protection and direct cellular effects. As a result of binding to CD44 receptors on chondrocytes, HA hinders the expression of catabolic enzymes such as matrix metalloproteinases (MMPs) and aggrecanases, which are responsible for cartilage degradation in osteoarthritis [10]. Concurrently, HA promotes anabolic activity by stimulating chondrocyte proliferation and the synthesis of specific extracellular matrix components, including proteoglycans and type II collagen [11]. These combined actions help preserve the proper structure of cartilage, reduce matrix breakdown, and promote tissue repair, forming the basis of HA's chondroprotective role in degenerative and overuse joint conditions.

5.3 Anti-Inflammation and Tissue-Regeneration

HA also exerts significant anti-inflammatory effects by modulating immune cell activity and inhibiting pro-inflammatory mediators. High-molecular-weight HA has been shown to suppress the production of interleukin-1β (IL-1β), tumor necrosis factor-alpha (TNF-α) [12], and prostaglandin E2 (PGE2), while also downregulating the activity of nuclear factor-kappa B (NF-κB) - a central transcription factor in inflammatory cascades [13]. These mechanisms help to reduce synovial inflammation and decrease cartilage catabolism, both of which are critical in halting the progression of degenerative joint diseases and minimizing pain in mechanically stressed joints.

Additionally, HA demonstrates tissue-regenerating properties, supporting cellular proliferation, migration, and matrix remodeling. It enhances wound healing by promoting angiogenesis and fibroblast activity, and also influences mesenchymal stem cell differentiation in the joint microenvironment [14]. These regenerative effects are highly relevant in musculoskeletal applications, where HA may contribute to soft tissue recovery following microtrauma or overuse injuries, such as tendinopathies and ligament sprains. The dual anti-inflammatory and pro-regenerative profile of HA is central to its growing role in regenerative medicine and biologic joint preservation strategies.

5.4 Analgesic and Pain Reliever

Moreover, HA enhances joint function and provides effective pain relief by improving lubrication and showing anti-inflammatory effects. Intra-articular HA has been shown to knowingly reduce pain and improve physical function in patients with knee osteoarthritis, as measured by validated scales such as WOMAC and KOOS [15]. This analgesic effect is achieved in part by restoring viscoelasticity, reducing friction, and modulating nociceptive nerve endings within the joint [1]. Studies further indicate that high-molecular-weight HA delivers longer-lasting pain relief and functional improvements compared to lower-molecular-weight formulations [16].

5.5 Moisture Retention and Hygroscopicity

HA is an inherently hygroscopic substance, capable of attracting and retaining large amounts of water due to its polyanionic structure and hydrogen bonding network. Reviews confirm that HA contributes meaningfully to extracellular matrix hydration and tissue viscoelasticity [1]. In synovial fluid, high-molecular-weight HA ensures an optimal osmotic balance, compressive resistance, and nutrient diffusion across articular surfaces, which are essential for cartilage function and health [17].

This hydration function supports both mechanical resilience and cellular metabolism within joint tissues. By maintaining an intensely hydrated extracellular environment, HA helps buffer compressive forces, reduce shear stress, and enable nutrient transport to chondrocytes, collectively preserving tissue integrity and contributing to improved joint homeostasis and durability.

6. Clinical Applications of HA

HA offers anti-inflammatory, lubricating, and tissue-repair properties among others, making it valuable in treating athletic injuries. In athletes, HA has demonstrated benefits across various conditions, including tendinopathies, sprains, and early joint degeneration, by reducing pain, improving function, and accelerating return to sport, all with high safety and tolerability.

6.1. Tendinopathies

6.1.1. Rotator Cuff / Supraspinatus Tendinopathy

In athletes with chronic supraspinatus tendinopathy, subacromial HA injections, combined with standard physiotherapy, significantly shortened rehabilitation time and reduced the number of sessions required. A multicenter randomized controlled trial (RCT) showed patients in the HA group returned to pre-injury activity approximately 12 days sooner than controls and demonstrated greater functional gains, with no increase in side effects [18]. A scoping review of HA use in rotator cuff tendinopathy confirmed consistent improvements in pain and shoulder function, with HA performing comparably or better than corticosteroids and showing excellent tolerability [19].

6.1.2. Patellar Tendinopathy

Peritendinous injections of HA have also shown clinical benefit for patellar tendinopathy. In a prospective study, both professional and semi-professional athletes with Blazina stage II-III patellar tendinopathy received high-molecular-weight HA injections into the tendon–fat pad interface. At an average follow-up of 25.7 months, 54% reported ‘excellent’ and 40% reported ‘good’ outcomes, with most athletes returning to their prior sports activities and experiencing minimal limitations [20]. Another open-label study, using medium–molecular–weight HA (500–730 kDa), administered under ultrasound guidance, showed that HA injections significantly reduced pain, decreased tendon thickness and vascularity on ultrasound, and proved to be a safe and tolerable treatment [21].

6.1.3. Achilles Tendinopathy

Additionally, peritendinous injections of HA into Achilles tendinopathies have demonstrated measurable improvements in biomechanics, pain, and function in athletes. In a pilot clinical study on recreational runners with unilateral Achilles tendinopathy, patients who received three ultrasound-guided peritendinous injections every 15 days presented significant reductions in interleukin-1β and MMP-3 levels, along with improved viscoelastic tone, isometric strength, and pain scores, compared to baseline [22]. In a separate prospective pilot study including patients with non-insertional mid-portion Achilles tendinopathy, a single ultrasound-guided peri-tendinous injection of 2% HA resulted in dramatic pain reduction. Mean Visual Analogue Scale (VAS) scores decreased from ~9.4 to ~3.0 at 12-week follow-up ($p<0.0001$), and functional scores measured via the Manchester-Oxford Foot Questionnaire (MOxFQ) improved by nearly 44 points. No significant complications were recorded, underscoring HA's safety and tolerability in this athlete-relevant cohort [23].

6.2. Acute Ankle Sprain

HA application is also investigated in the treatment of acute ankle sprains. A high-quality RCT involving 158 competitive athletes with acute grade I or II lateral ankle sprains found that peri-articular HA injections, administered within 48 hours and again at day 4 alongside standard RICE therapy, produced significantly greater pain reduction by day 8 compared with placebo ($P < 0.001$) and shortened the mean time to pain-free, disability-free return to sport from 17 ± 8 days in the placebo group to 11 ± 8 days in the HA group ($P < 0.05$). Long-term follow-up (up to 24 months) also revealed fewer reinjuries with high patient satisfaction and no serious adverse events [24]. Another systematic review assessed the effectiveness of HA injections across multiple soft tissue foot and ankle pathologies, including acute lateral ankle sprains in athletic cohorts. The analysis included data from 119 patients across two studies concentrating on athletes with ankle sprains. Results demonstrated significant pain and functional improvements, a failure rate of 0%, and an overall complication rate of approximately 2.5%, all with HA-based interventions. The review supports HA's favorable safety profile and consistent benefits in sport-related ankle sprains - particularly in athletes aiming for a rapid return to function [25].

6.3 Early Knee Injuries

In cases of early knee trauma, such as anterior cruciate ligament (ACL) reconstruction and meniscal injury, intra-articular HA has been utilized to support recovery in athletes and active individuals. A randomized, controlled clinical trial administered three weekly HA injections starting two weeks after ACL reconstruction. The HA group showed significantly greater improvements in Lysholm scores, knee range of motion, ambulatory speed, and quadriceps/hamstring peak torque at 4–16 weeks compared to controls receiving saline ($P < 0.05$). The most pronounced benefits were noted in participants receiving HA at 8 weeks post-op, including superior outcomes at one-year follow-up [26]. Another randomized controlled study evaluated a novel HA-derived hydrogel in patients with meniscal lesions who are active in sports. The study demonstrated significant improvements in pain, function, and a reduction in the length and depth of meniscal lesions compared to control groups [27].

6.4. Early Joint Degeneration and Osteoarthritis

Athletes, despite their youth and high fitness, are at risk of accelerated joint degeneration, particularly following repetitive loading, cartilage microtrauma, or prior meniscal or ligament injuries. Intra-articular HA has been utilized as a non-operative modality to manage early knee osteoarthritis (OA) in active individuals aiming to delay more invasive interventions. A study of active football players with early knee OA showed that intra-articular HA injections provided rapid pain relief and improved function, as well as good toleration and no adverse effects, enabling an early return to sports activity [28]. In a prospective study of professional soccer players with knee chondropathy, two intra-articular injections of HYADD4-G, which is a modified form of HA, resulted in significant reductions in pain and improvements in KOOS scores at 1, 3, and 6 months post-treatment. All athletes returned to play by 6 months, with no adverse effects, supporting both the efficacy and safety of HA in elite sports settings [29].

7. Limitations

Although HA shows promising results in treating various musculoskeletal injuries in athletes, unfortunately, its clinical applications are not without limitations.

To begin with, many studies in this population are non-randomized, small-scale, or lack long-term follow-up, which limits the generalizability of their findings. For example, although studies have reported improvements in symptoms of Achilles tendinopathy or patellar tendinopathy after HA injections [20, 22], sample sizes are often limited, and outcomes are based on short-term assessments.

Additionally, variability in HA formulations (e.g., low vs. medium MW at 500–730 kDa, high MW 2% concentrations), injection sites (peri-tendinous vs. intra-articular), and guidance methods (ultrasound vs. palpation) complicate cross-study comparisons and hinder establishment of standardized regimens [21, 23].

Although HA is generally well-tolerated, transient local reactions, such as injection-site pain, swelling, or mild inflammatory responses, have been reported. For athletes, even brief periods of inflammation or discomfort can interrupt training and competition schedules [30].

Moreover, HA injections, especially in regimens requiring multiple sessions [31], can be expensive and time-consuming. This raises questions about cost–benefit balance for athletes faced with repeated treatments.

8. Future Directions

As the applications of HA become increasingly common within sports medicine, several important gaps and emerging future research pathways should be identified.

While current evidence highlights the therapeutic potential of HA, future studies should also explore its preventive applications. Administering HA prophylactically in athletes with early degenerative changes, repetitive joint overload, or a history of injury may potentially help delay progression of subclinical cartilage wear (e.g., chondromalacia) or early tendinopathy. Such a strategy could mirror preventive models employed in high-risk sports, such as long-distance running or football.

Current studies often focus on generic pain or functional scores. To better capture the athletic significance, future trials should also prioritize return-to-sport timelines and time-to-peak performance. These outcomes would provide more meaningful data for people working in sports, such as physicians and coaches.

Moreover, sport-specific biomechanics should also be taken into consideration. Different disciplines impose distinct loads on joints and soft tissues, which can potentially influence the efficacy of HA. For example, evaluating whether HA injections benefit sprinters with Achilles tendinopathy more than weightlifters or volleyball players could lead to the development of tailored interventions.

Additionally, female and adolescent athletes remain noticeably underrepresented in current studies evaluating the use of HA. Given known differences in joint laxity, hormonal influences, and injury patterns, future research should place greater emphasis on understanding how sex and age-specific variables impact the outcomes of HA therapy.

Finally, although HA is not a direct treatment for psychological aspects of injury, its role in accelerating recovery may indirectly support mental resilience and motivation. Incorporating psychometric assessments, such as anxiety, confidence, or mood, into future trials may offer a more holistic understanding of HA's impact on athletic rehabilitation.

9. Discussion and Conclusions

HA has emerged as a valuable therapeutic option in sports medicine, particularly for athletes seeking minimally invasive treatments that allow rapid recovery and sustained joint health. Its biological properties, ranging from lubrication and viscoelasticity to anti-inflammatory and chondroprotective effects, support its diverse clinical applications across tendon, ligament, and early degenerative joint changes.

In athletic populations, HA has consistently shown benefits in reducing pain, improving function, and facilitating an earlier return to sport following conditions such as rotator cuff tendinopathy, patellar and Achilles tendinopathies, acute ankle sprains, and early osteoarthritis. Moreover, due to its safety profile and low incidence of adverse effects, it is perceived as an attractive replacement to corticosteroids or surgical interventions. These results, observed in both professional and recreational athletes, highlight the value of HA in addressing the high functional demands of sports-related injuries.

Despite these promising outcomes, current evidence is not without its limitations. Many of the existing studies in athletic cohorts are short-term, underpowered, and heterogeneous, with inconsistent use of HA formulations, dosages, and administration techniques. These factors hinder robust comparisons and the formulation of sport-specific treatment protocols. Furthermore, outcomes are often limited to subjective pain scales, while return-to-play metrics and long-term structural joint preservation remain under-investigated. Questions about cost-effectiveness and preventive use also remain largely unanswered.

Moving forward, high-quality, sport-specific clinical trials with long-term follow-up are needed to validate HA's role in performance restoration and joint preservation. There is a particular need to include diverse athletic populations, such as youth athletes, female athletes, and those participating in underrepresented sports, to understand variations in response better. Additionally, incorporating objective biomechanical outcomes, imaging, and psychological recovery measures will enrich our understanding of HA's broader impact on athletic performance and health.

In conclusion, HA represents a promising and biologically rational approach for treating musculoskeletal injuries in athletes. While existing studies support its safety and short-term efficacy, further research is needed to standardize protocols, determine long-term outcomes, and fully explore its potential as both a therapeutic and preventive strategy in sports medicine.

Disclosures

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