

Intra-articular hyaluronic acid plus sorbitol injections for the management of severe glenohumeral osteoarthritis in a former female volleyball player: A case report

 **Domiziano Tarantino**  . Department of Public Health. University of Naples Federico II. Italy.
 **Rossana Gnasso**. Department of Public Health. University of Naples Federico II. Italy.
 **Felice Sirico**. Department of Public Health. University of Naples Federico II. Italy.
 **Bruno Corrado**. Department of Public Health. University of Naples Federico II. Italy.

ABSTRACT

The glenohumeral joint is the third most common joint to be affected by osteoarthritis (OA). Practising volleyball can lead to shoulder arthritis due to repetitive mechanical stress on the shoulder joint. The first step of management of primary glenohumeral OA usually is the non-operative treatment, with intra-articular injections representing one of the most utilized treatments. The aim of this study is to report the outcomes of a series of three injections of hyaluronic acid (HA) plus sorbitol in a patient with severe glenohumeral OA. An 81-year-old female former volleyball player presented to our Rehabilitation Unit with more than 15 years history of shoulder pain and functional limitation. Since she refused to undergo surgery, we proposed her intra-articular injections of HA plus sorbitol. Outcome evaluation was made up to 12 months from the last injection by means of the Constant-Murley score and the Disability of the Arm, Shoulder and Hand questionnaire. Three injections of HA plus sorbitol for three weeks in a row in a patient with severe glenohumeral OA led to important improvements in pain reduction and better functionality at all follow-ups. Larger studies including more patients and with longer follow-ups are needed to confirm the consistency of these findings.

Keywords: Sport medicine, Glenohumeral osteoarthritis; Hyaluronic acid; Intra-articular injections; Osteoarthritis; Sorbitol.

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 **Corresponding author.** Department of Public Health. University of Naples Federico II. Italy.

E-mail: domiziano22@gmail.com

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INTRODUCTION

Osteoarthritis (OA) is the most common joint disease worldwide, involving approximately the 15% of the worldwide population (Johnson and Hunter, 2014). The number of people affected by symptomatic OA is constantly rising due to the aging of the population and the global obesity epidemic (Neogi and Zhang, 2013). OA is a leading cause of disability and can affect people's physical and mental well-being. Healthcare resources and costs employed with managing the disease are considerable (Vina and Kwok, 2018).

The glenohumeral joint is the third most common large joint to be affected by OA, following the knee and the hip (Ansok and Muh, 2018). Population-based studies showed that the 16.1%-20.1% of adults older than 65 years have radiographic evidence of glenohumeral OA (Oh et al., 2011). Glenohumeral OA is a multifactorial disease (Man and Mologhianu, 2014), with risk factors including ageing, female sex, obesity, rheumatic diseases, avascular necrosis, prior trauma or surgery, and participating in sports.

For example, shoulder arthritis is one of the most common injuries of professional volleyball players. It needs shoulder force to buckle, block, and bounce, which leads to frequent shoulder injuries (Cui, 2022).

Over time, glenohumeral OA results in worsening pain and stiffness, yielding functional limitations and decreased quality of life. Patients often complain of insomnia or difficult awaking due to the night pain, severely impacting the quality of life and the psychological health (Cho et al., 2017). Early glenohumeral degeneration is a difficult condition for the competing athlete who participate in overhead sports such as volleyball, and this may lead to impaired performance, and, ultimately, derailed careers (Reineck et al., 2008).

Patient's anamnesis, a careful clinical exam and radiographs are the keystone of a correct diagnosis and staging of glenohumeral OA. Radiographs usually show joint space narrowing and posterior glenoid wear. Subchondral sclerosis and osteophytes from the humeral head, often described as a "goat's beard", can also be present (Kircher et al., 2014).

The first step of management of primary glenohumeral OA usually is the non-operative treatment (Ansok and Muh, 2018). Drugs, such as paracetamol, nonsteroidal anti-inflammatory drugs (NSAIDs) and corticosteroids are commonly used (Ansok and Muh, 2018).

Intra-articular injections represent one of the most utilized non-operative treatments for glenohumeral OA, especially using corticosteroids and hyaluronic acid (HA), for which there are multiple formulations (Ansok and Muh, 2018). Several studies reported good outcomes in terms of pain and functionality with the use of HA at short-term and long-term follow-ups (Blaine et al., 2008; Brander et al., 2010; Colen et al., 2014; Di Giacomo and De Gasperis, 2015; Merolla et al., 2011).

Anyway, while the use of HA in the shoulder has been approved by the European Medicines Agency since 2007, the Federal Drug Administration has approved its use only in knees. For this reason, while the effects of HA injections are well studied for the treatment of knee OA, the effects on glenohumeral OA are still under discussion, even if several studies reported good outcomes in terms of pain and functionality at short-term and long-term follow-ups.

High affinity between HA and sorbitol stabilizes the complex through a very dense network of hydrogen bonds that do not modify the visco-elastic properties of HA (Conrozier, 2018). The strong ability of sorbitol to scavenge and neutralize oxygen free radicals has been demonstrated to delay degradation of the gel.

Moreover, neutralizing free radicals decreases migration of macrophages into the synovial membrane reducing inflammation, pain and oxidative stress-induced chondrocyte apoptosis (Migliore et al., 2014; Mongkhon et al., 2014). Furthermore, the penetration of the HA/sorbitol complex in the cartilage could represent a major mechanism explaining its long-term efficacy (Lavet et al., 2017).

Given these interesting *in vitro* findings related to the use of a combination of HA plus sorbitol and given the lack of clinical studies about the infiltrative treatment of shoulder OA using this kind of viscosupplement, in this study we wanted to report the outcomes of a series of three injections of HA plus sorbitol in a patient with severe glenohumeral OA who was not eligible for surgery.

MATERIAL AND METHODS

In December 2021, an 81-year-old former female volleyball player presented to the outpatient Clinic of the Rehabilitation Unit, Department of Public Health, University of Naples Federico II, Italy, with >15 years history of important right shoulder pain and functional limitation. She did not report neither systemic nor genetic disorders, nor history of allergies or intolerances. She did not experience any traumatic events or surgical interventions involving her right shoulder. She did not smoke. Her body mass index was 24. The patient underwent conservative treatments for years including relative rest, multiple rounds of NSAIDs and formal physical therapy, with some relief of her symptoms. Since her shoulder pain increased in severity and intensity over the last months, limiting her activities of daily living and keeping her awake at night causing significant sleep deprivation, she booked a medical appointment at our outpatient Clinic.

At the time of the medical consult, patient's VAS was 7/10, the Constant-Murley score (CMS) was 29/100, and the disability/symptom section' score of the Disability of the Arm, Shoulder and Hand (DASH) was 52%.

According to the Kellgren and Lawrence classification system, true antero-posterior radiograph showed a grade 4 (severe) glenohumeral OA with marked narrowing of the joint space, along with severe sclerosis, large osteophytes, and definite deformity of bone ends (Figure 1).

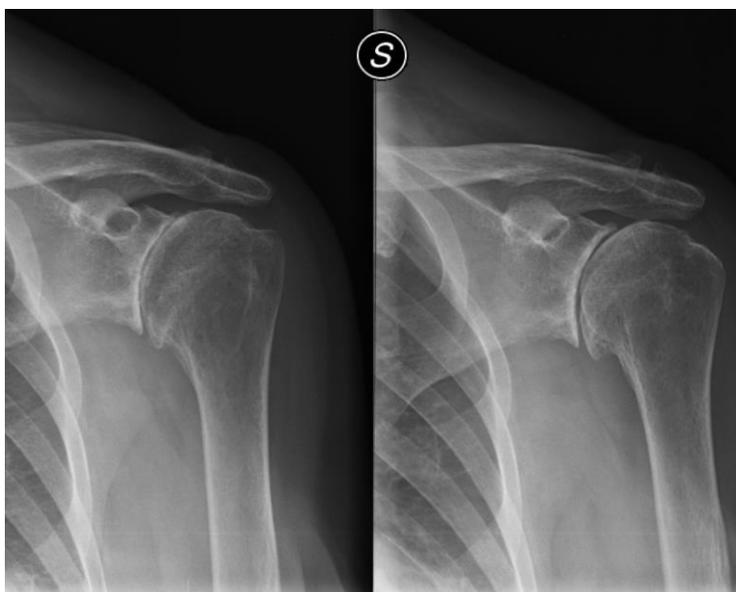


Figure 1. Radiograph obtained few days before the first medical appointment.

At physical examination, reduced ranges of movement and arm strength were found. According to the Management of Glenohumeral Joint Osteoarthritis Evidence-based Practice Guideline adopted by the American Academy of Orthopaedic Surgeons (AAOS) [18,19], the patient received indications for anatomic total shoulder arthroplasty. Then, to provide her some relief, we planned a series of three intra-articular injections of 2ml, high concentrated (20 mg/ml) 2 million Dalton (mDa) HA of non-animal origin, combined with high concentrated (40 mg/ml) sorbitol, once a week for three weeks in a row. After a full and clear description of the procedure, the patient was invited to sign the informed consent. Written informed consent for publication was also obtained prior to the intervention and data collection.

All injections were performed by a single doctor (B.C.) with >10 years of experience using an ultrasound-guided posterior approach with a 22-gauge needle. The patient was asked to rest her arm for 12 hours after each injection. No limitations on physical performance and daily activities were suggested for the rest of the time.

The patient was evaluated at the time of enrolment (T0) that was also the day of the first performed injection, at one month (T1), three months (T2) and 12 months (T3) after the last injection by means of the CMS and the DASH-disability/symptom section score.

The patient was totally compliant, following all the appointments given. No adverse events were described after HA injections.

RESULTS

Clinical data are reported in Table 1 and their trends are illustrated in Figure 2.

Table 1. CMS and DASH scores' trends on follow-ups.

	T0	T1	T2	T3
CMS	29 (13+16)	76 (30+46)	56 (24+32)	50 (18+32)
DASH (%)	52	12	10	13

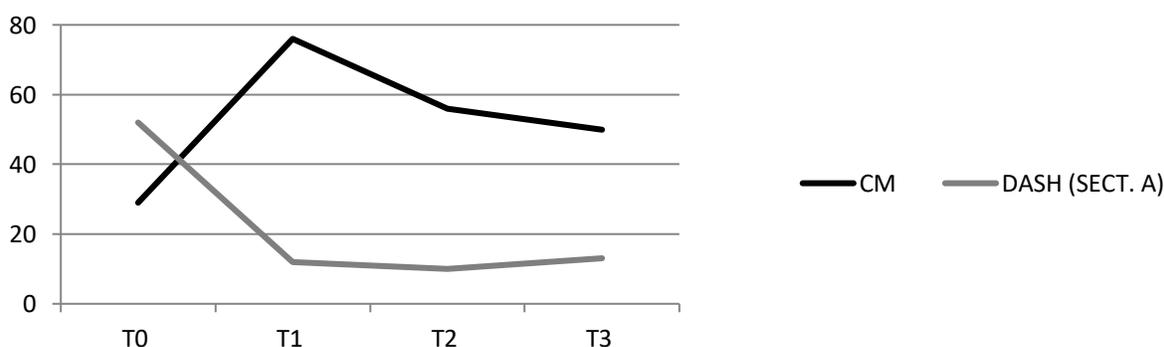


Figure 2. Graphical representation of CMS and DASH scores' trends on follow-ups.

At the time of enrolment (T0), the CMS was 29 (13+16), while the DASH score (referred to the disability/symptom section) was 52%.

One month after the last injection (T1), the CMS was 76 (30+46), while the DASH score (referred to the disability/symptom section) was 12%.

Three months after the last injection (T2), the CMS was 56 (24+32), while the DASH score (referred to the disability/symptom section) was 10%.

Twelve months after the last injection (T3), the CMS was 50 (18+32), while the DASH score (referred to the disability/symptom section) was 13%.

Regarding the CMS, the score increased from the baseline (T0) to T1 by 162%. After three months (T2), the score started to decrease, reporting a worsening of the 26% if compared to T1. From T2 to T3, the score further decreased, reporting a worsening of the 11%. Anyway, if compared to T0, the score at T3 increased by the 72%.

Regarding the DASH score (referred to the disability/symptom section), the score decreased from the baseline (T0) to T1 by 77%. After three months (T2), the score further decreased, reporting an improvement of the 17%. From T2 to T3, the score slightly increased, reporting a worsening of the 30%. Anyway, if compared to T0, the score at T3 decreased by the 75%.

DISCUSSION

Intra-articular injections of HA are one of the most used conservative treatments for OA. In this study, we wanted to investigate the effects of a series of three injections of HA plus sorbitol in a former female volleyball player with severe glenohumeral OA who was not eligible for surgery.

The results of our case-report showed noticeable improvements in shoulder pain reduction and improved functionality. These improvements were observed during the entire duration of follow-ups, with the higher improvement found at 1-month follow-up, with the CMS increasing from T0 to T1 by 162% and the DASH-disability/symptom section increasing from T0 to T1 by 77%.

Several studies in the available scientific literature evaluated the effects of intra-articular injections of HA in patients with glenohumeral OA.

A recent systematic review and meta-analysis by Zhang et al. (2019) analysed the efficacy of intra-articular HA administration on pain reduction in patients with glenohumeral OA. Fifteen studies, for a total of 1594 patients, were included in the review. The authors found significant reduction in pain at three and six months for patients receiving intra-articular HA injections for glenohumeral OA. Furthermore, improved functional outcomes at every follow-up time point were noticed across all the included studies. The authors concluded that HA injections for glenohumeral OA are safe and improve pain.

Few studies evaluated the effects of the association of HA and sorbitol, and almost all of them were conducted for knee OA.

A non-interventional study by Heisel and Kipshoven (2013) was conducted to assess the efficacy and tolerability of one, two or three intra-articular injections of a 2ml of high concentration (20 mg/ml) of a 2 mDa HA, combined with high concentration (40 mg/ml) of sorbitol for the treatment of OA. A total of 1147 patients were enrolled. The most treated joint was the knee (92.9%), followed by the hip (4.4%), and the shoulder (2.8%). Pain was assessed with Likert scale and went toward a reduction of 56.5% from baseline to six-month follow-up. Adverse reactions were rare, and no infections were reported.

Migliore et al. (2014) evaluated the efficacy of HA plus sorbitol injections for the treatment of symptomatic hip OA in a study prospective, non-controlled clinical trial. A total of 20 patients were enrolled in the study and received a single, ultrasound-guided injection of the hip with 4 ml of high concentration (20 mg/ml) of a 2 mDa HA, combined with high concentration (40 mg/ml) of sorbitol. Results were evaluated at three, six, nine and twelve months by means of several assessment tools. Mean scores of all clinical parameters were significantly different compared with the baseline mean value at each follow-up, and no systemic adverse effects were observed.

In a recent prospective cohort study by Cucurnia et al. (2021), a total of 77 patients with symptomatic knee OA were treated with a single intra-articular injection of a 4 ml of high concentration (20 mg/ml) of a 2 mDa HA, combined with high concentration (40 mg/ml) of sorbitol. Pain, stiffness, functional limitation, and total scores were significantly reduced at one, three and six months, but not at 12 months. Their results showed better outcomes in patients with a low-grade OA, but this finding was not in agreement with the one found also recently by Bruyère et al. (2021), who stated that that a more limited physical function at baseline was associated with more important function relief.

CONCLUSIONS

In our study, we decided to treat the patient using a HA plus sorbitol viscosupplement given the good outcomes reported by the above-mentioned studies, even if almost all studies were conducted for knee OA. Three injections of HA plus sorbitol for three weeks in a row in a patient with severe glenohumeral OA who was non-eligible for surgery led to important improvements in pain reduction and better functionality.

The clinical and functional improvements observed during the entire duration of follow-ups (with the higher improvement found at 1-month follow-up), together with the absence of side effects and the improvement of patient's quality of life, allow us to propose HA plus sorbitol viscosupplement as a safe and effective treatment for glenohumeral OA.

Larger studies including a consistent number of patient and with longer follow-ups are needed to confirm the consistency of these findings.

AUTHOR CONTRIBUTIONS

Domiziano Tarantino: methodology, investigation, writing, review and editing. Rossana Gnasso: data collection, investigation, review and editing. Felice Sirico: methodology, investigation, writing, review and editing. Bruno Corrado: data collection, methodology, investigation, writing, review and editing.

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DISCLOSURE STATEMENT

The Authors state that the methodology for this study is in accordance with the Declaration of Helsinki, and followed the guidelines given by the local ethics committee.

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