

[Primary Care]

Glenohumeral Joint Injections: A Review

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Context: Intra-articular injections into the glenohumeral joint are commonly performed by musculoskeletal providers, including orthopaedic surgeons, family medicine physicians, rheumatologists, and physician assistants. Despite their frequent use, there is little guidance for injectable treatments to the glenohumeral joint for conditions such as osteoarthritis, adhesive capsulitis, and rheumatoid arthritis.

Evidence Acquisition: We performed a comprehensive review of the available literature on glenohumeral injections to help clarify the current evidence-based practice and identify deficits in our understanding. We searched MEDLINE (1948 to December 2011 [week 1]) and EMBASE (1980 to 2011 [week 49]) using various permutations of *intra-articular injections* AND (*corticosteroid* OR *hyaluronic acid*) and (*adhesive capsulitis* OR *arthritis*).

Results: We identified 1 and 7 studies that investigated intra-articular corticosteroid injections for the treatment of osteoarthritis and adhesive capsulitis, respectively. Two and 3 studies investigated the use of hyaluronic acid in osteoarthritis and adhesive capsulitis, respectively. One study compared corticosteroids and hyaluronic acid injections in the treatment of osteoarthritis, and another discussed adhesive capsulitis.

Conclusion: Based on existing studies and their level of evidence, there is only expert opinion to guide corticosteroid injection for osteoarthritis as well as hyaluronic acid injection for osteoarthritis and adhesive capsulitis.

Keywords: glenohumeral; arthritis; injection; corticosteroid; hyaluronic acid

Shoulder disorders are a cause for significant morbidity, with a prevalence of 6.9% to 34% in the general population and up to 21% in those over 70 years old.¹⁵ These debilitating disorders present a challenge to the treating clinician; conservative treatment options are finite before surgery is indicated. Current modalities include physical therapy, corticosteroid injection, viscosupplementation with hyaluronic acid (HA), nonsteroidal anti-inflammatory drugs (NSAIDs), and glucosamine and chondroitin sulfate. The success of these therapies may in part be based on the self-limiting nature of conditions such as adhesive capsulitis.

Shoulder injections of corticosteroids and HA are not limited to the glenohumeral joint. Rather, they are used in conditions of the subacromial space, acromioclavicular joint, bicipital tendon sheath, sternoclavicular joint, and the subcoracoid bursa.⁵¹ Though the use of HA is approved by the Food and Drug Administration for intra-articular injections in the knee, it remains an off-label use in the shoulder and its surrounding spaces. In this review, intra-articular injections to the pathologies affecting the glenohumeral joint are addressed with focus on corticosteroids and viscosupplementation.

The accuracy of injection delivery to the glenohumeral joint proper has been unreliable.⁵⁵ Tobola et al⁵⁵ examined the accuracy of intra-articular injection utilizing anterior, supraclavicular, and posterior approaches. Differences among these approaches were not significant; the anterior approach had a reliability of 64.7%, compared with 45.7% and 45.5% for supraclavicular and posterior approaches, respectively. However, anatomic delivery of injectable medications into the glenohumeral joint may not be relevant.²⁶ Hegedus et al found that relief of shoulder pain with injectables did not correlate with clinician experience, injection intra- or extracapsularly, and duration of symptoms.²⁶

CORTICOSTEROIDS

Injectable steroids have been in use for decades to treat various disorders of the glenohumeral joint.³ Much of the evidence supporting the use of corticosteroids is anecdotal. Indeed, level 1 and 2 evidence supporting the use of intra-articular corticosteroids is lacking. Confounding variables such as physiotherapy, analgesics, and NSAIDs also make it difficult to arrive at definitive conclusions or recommendations.³

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Table 1. Injectable corticosteroid properties.

Generic Name: Trade Name	Dose, mg ¹⁷	Solubility, % wt/vol ²⁰	Mean Duration of Action, d ^{5,23}	Fluorinated
Methylprednisolone diacetate: Depo-Medrol	40-60	.001	7-84	No
Prednisolone tebutate: Hydeltra-TBA	5-50	.001	10-15	No
Triamcinolone acetonide: Kenalog	5-40	.004	11	Yes
Triamcinolone hexetidine: Aristospan	5-40	.0002	3	Yes
Betamethasone sodium phosphate, betamethasone acetate: Celestone Soluspan	1.5-6	NA	9	Yes

Properties

The pharmacologic properties of corticosteroids have been well documented.^{10,23} They act locally and are much like the anti-inflammatory effects of systemic steroids^{10,23} In the knee, local lymphocytes, macrophages, mast cells, and overall edema of the joint after injection with Depo-Medrol occurs.⁴⁵ Local corticosteroid injection also decreases the erythrocyte- sedimentation rate and C-reactive protein in patients with rheumatoid arthritis.¹⁶

The injectable formulations vary by molecular size, crystal structure, serum half-life, solubility, fluorination, and duration of action.¹⁶ Water-soluble steroids (dexamethasone) rapidly dissipate from the joint and exert many systemic side effects.¹⁶ These are primarily helpful with extra-articular uses such as carpal tunnel. Conversely, formulations with lower solubility maintain longer synovial levels with decreased systemic effects.¹⁶ The length of action for each steroid varies widely among different corticosteroids (Table 1).^{5,10,23} While decreased solubility maintains longevity within the synovium, solubility is not correlated to duration of action.⁴⁶ The chemical structure of the steroid also affects activity: fluorinated compounds (Decadron, Kenalog, Aristospan, Celestone) have increased activity and systemic absorption⁴² and a higher rate of side effects. Moore suggests that the use of fluorinated compounds be limited to intra-articular injections because of the higher rate of tendon rupture and subcutaneous collagen atrophy.³⁹ Flocculation (colloids out of solution) can also occur with the mixture of corticosteroids and local anesthetic agents and may inhibit the local effects of the steroid.

The most effective dosage and specific type of corticosteroid are not known (Table 1). Recommendations for the frequency of intra-articular injection are empirically based on the recommendations of the American College of Rheumatology.²⁵ Generally, a steroid should not be injected into the same joint more than every 3 months.²⁵ Aspirating synovial fluid at the time of injection and resting the joint may decrease painful relapses.^{13,19}

Side Effects and Complications

The complication rate of intra-articular corticosteroid injections is relatively low (1%-15%).²⁵ One of the most common complications is transient pain during injection and/or postinjection (6.7%). Flare-up pain usually lasts 24 to 48 hours and most likely results from a transient reactive synovitis in response to the steroid crystals. Facial flushing may occur in up to 15% of patients, with a greater number of women affected. The effects are transient, lingering for no more than 3 days.³³ Skin or subcutaneous fat atrophy may occur after corticosteroid injection and may persist longer than 6 months (.35%).³² Septic arthritis is the greatest concern, occurring from 1:3000 to 1:50 000.¹⁴ Hyaline cartilage damage has been reported in animal models but not in humans.¹⁶ Contraindications to intra-articular corticosteroid injection include a prosthetic joint, septic arthritis, and joint fracture.³²

The hypothalamic pituitary-adrenal axis may be suppressed with corticosteroids injected locally. A single intra-articular injection of methylprednisone acetate showed an average 21.5% reduction in serum cortisol 24 hours after injection normalizing in 3 days.³⁴

Glenohumeral Arthritis

The glenohumeral joint is the third-most-common large joint affected by degenerative joint disease.³⁷ It is usually diagnosed at much later stages of disease and less frequently than knees or hips. Conservative management for glenohumeral arthritis includes activity modification, physical therapy to promote strength and flexibility, nonnarcotic medications to reduce pain, intra-articular corticosteroid injections to reduce local inflammation, viscosupplementation, and general health maintenance.⁴⁴

There is currently no level 1 or 2 studies on intra-articular corticosteroid injections as a treatment modality for glenohumeral arthritis.²⁹ While literature suggests that injectable corticosteroid therapy is a treatment modality for shoulder arthritis, not one lists shoulder-specific evidence.

Table 2. Study characteristics of hyaluronic acid and corticosteroid use for arthritis.

Study	Type	Patients, n	Follow-up, wk	Treatment Arm	Control Arm	Outcomes Measures
Merolla ³⁸	Retrospective controlled	84	26	Hylan G-F 20	Methylprednisolone acetate	Constant-Murley, Shoulder Pain and Disability Index, satisfaction

According to the most recent guidelines⁵⁴ for the treatment of glenohumeral arthritis, by the American Academy of Orthopaedic Surgeons, the use of injectable corticosteroids is inconclusive. Unfortunately, the organization is unable to recommend for or against glenohumeral corticosteroid injections.⁵⁴ One study does address corticosteroids in comparison to HA in treating shoulder osteoarthritis.³⁸ This is discussed in the HA section (Table 2).

The use of corticosteroids in glenohumeral arthritis is based on its effects on the synovium and surrounding tissue, as well as its clinical efficacy in other arthroal joints, especially the knee.⁶ Triamcinolone hexetidine injection in knee osteoarthritis⁹ showed improved visual analog pain scale at 1 week compared to placebo. An intra-articular injection of methylprednisolone acetate demonstrated a significant reduction in pain at 3 weeks.³⁰ However, at 6 to 8 weeks, no appreciable difference was seen in either steroid. A more successful response was seen in patients with an intra-articular effusion and aspiration of synovial fluid at the time of injection.³⁰ A 24-month randomized trial with triamcinolone acetate injection of symptomatic knees every 3 months noted improvement in range of motion and slightly improved pain at 1 year.⁴⁷ Patients in the steroid group had improved knee pain and stiffness and no difference in joint space at the end of 2 years.

Adhesive Capsulitis

Adhesive capsulitis (frozen shoulder) affects 2% to 5% of the adult population.⁴¹ It may be idiopathic or present after shoulder immobilization, trauma, or surgery.⁵⁶ It may be intrinsic (tightening of the joint capsule) or extrinsic (scarring of the rotator interval or external rotators). It is usually self-limiting and has 3 phases: freezing, frozen, and thawing.⁵⁶ In the first stage, capsular inflammation occurs⁸; consequently, intra-articular corticosteroid injections are thought to be best during this initial phase. In a systematic review of corticosteroid injections compared with physical therapy in the treatment of adhesive capsulitis, greater improvements in shoulder pain and function in the short term are reported with glenohumeral joint corticosteroid injections versus physical therapy (Table 3).⁸ Greater efficacy of glenohumeral corticosteroid injections compared with physical therapy⁵⁷

persisted at 1 year and were more beneficial than physical therapy and NSAIDs combined.⁴

The dose of steroid affects the outcome of adhesive capsulitis. Glenohumeral injection of 40 mg triamcinolone acetate (vs 10 mg)¹⁸ relieved more pain at 6 weeks. Arm function and glenohumeral range of motion improved, while sleep disturbances were unchanged.⁶¹

The data for corticosteroid treatment versus placebos or traditional oral medication are sparse. Studies comparing corticosteroid injection to lidocaine injection⁴⁸ have mixed results. In a double-blind intention-to-treat analysis at 6 months, there were no differences in range of motion or pain in the corticosteroid or lidocaine injection group.⁴⁸ In an unblinded study comparing steroid injection to NSAID therapy, glenohumeral injection reduced pain more than analgesia alone at 6 weeks.^{35,48} Interestingly, the location of injection was not a determinant of clinical effect; a steroid injection into the bicipital tendon sheath also provided pain relief. A systematic review of existing level 1 and 2 evidence comparing injectable steroids and no treatment, ice pack, or low volume of intra-articular saline solution showed that the corticosteroid group provided earlier return of shoulder motion and improvement in Shoulder Pain and Disability Index scores, but at 52 weeks, there was no difference between the groups.²⁴

HYALURONIC ACID

Hyaluronic acid is a high-molecular weight glycosaminoglycan composed of repeating disaccharide units of glucuronic acid and N-acetyl-glucosamine.^{9,52} The viscoelastic properties of HA play a critical role in joint mechanics in synovial fluid.^{9,50,52,59} Exogenous HA has anti-inflammatory, anabolic, analgesic, and chondroprotective effects.^{28,40}

Properties

In animal models, HA preparations with high molecular weight have increased efficacy.²⁷ Though proven to have anti-inflammatory and analgesic effects, the precise mechanism for pain relief is not known, given that it has a short half-life in the joint.^{21,40} The temporary improvement of normal viscoelastic joint properties likely contributes to pain relief, but it is unclear if HA

Table 3. Study characteristics of corticosteroid treatment of adhesive capsulitis.^a

Study	Type	Patients, n	Follow-up, wk	Treatment Arm	Control Arm	Outcomes Measures
Arlsan ⁴	RCT	20	2, 12	40 mg, methylprednisolone	NSAIDs, PT	VAS, ROM
Blanchard ⁸	SR	362	Up to 52	Triamcinolone or methylprednisolone	PT	VAS, ROM, SPADI, SF-36
de Jong ¹⁸	RCT	25	1,3,6	40 mg, triamcinolone	10 mg, triamcinolone	Pain, sleep disturbance
Griesser ²⁴	SR	409	Up to 52	Triamcinolone or methylprednisolone	PT, oral steroid, manipulation, ice pack, no treatment	SPADI, VAS, SF-36, ROM
Rizk ⁴⁸	RCT	48	3	40 mg, methylprednisolone	Lidocaine, PT	Pain, ROM
van der Windt ⁵⁷	RCT	109	3, 7, 13, 26, 52	40 mg, triamcinolone (no more than 3 injections)	12 sessions of PT	VAS day and night, passive lateral rotation and abduction

^aRCT, randomized controlled trial; SR, systematic review; NSAIDs, nonsteroidal anti-inflammatory drugs; PT, physical therapy; VAS, visual analog scale; ROM, range of motion; SPADI, Shoulder Pain and Disability Index.

anti-inflammatory effects contribute to viscosupplementation long-term relief. HA may coat the articular cartilage and prevent loss of essential chondrocyte matrix molecules, such as prostaglandins.⁴⁰ Exogenous HA may facilitate the de novo synthesis of HA.^{2,40} The interplay between mechanical and biological effects likely contributes to the difficulty in assessing the therapeutic effect for viscosupplementation. While the use of viscosupplementation in joints other than the knee has not yet been approved by the Food and Drug Administration, recent clinical studies have begun to address its potential use in the hip, ankle, and, more recently, the shoulder.^{50,52}

Side Effects and Complications

The side effect profile of viscosupplementation includes acute local reactions (pain and swelling in the joint within 72 hours), flare-up of pseudogout, and pseudosepsis (acute systemic inflammatory reactions).^{22,36,60} In a series of 4253 injections, acute local reactions occurred at a rate of 2.4%³¹; another study reported adverse reactions in 1.2% per injection or 5.2% per patient in a series of 1489 injections.⁵⁸ Higher molecular weight HA preparations have been shown to be safer with a decreased infection rate, since lower weight preparations require more frequent treatment to achieve the same clinical result.¹ Preparations that include HA derived from rooster combs may have increased immunogenicity and may account for the few cases of pseudosepsis in patients.⁶⁰

Several publications conflict on whether rates of adverse reactions are increased in patients with repeat injections of

HA.^{36,58,60} While some studies report an eightfold increase in adverse reactions in subsequent injections, others show adverse reaction rates less than those from the first series of injections.^{36,60} Another series reports the incidence of treatment-related adverse reactions to be 0.8% (3.4% of patients) in the first series, 4.3% (13.1%) in the second, and 5.4% (17.3%) in the third.⁵⁸

Glenohumeral Osteoarthritis

Patients with glenohumeral osteoarthritis treated with HA had a significant decrease in pain and significant improvements in activities of daily living, based on visual analog scale, University of California–Los Angeles, and Simple Shoulder Test scores (Table 4).⁵⁰ More patients slept comfortably after treatment (56%) than before (15%). However, the authors were unable to conclude which patients would benefit from HA therapy. Another prospective trial showed that at 3 months, the visual analog scale significantly decreased from 61.2 to 37.1 after 1 or 2 injections of HA.⁴³

In a multicenter, randomized, double-blind, controlled trial,⁷ the efficacy and safety of intra-articular injections of sodium hyaluronate (molecular weight, 500 to 730 kDa) for persistent shoulder pain and limited function, including glenohumeral joint arthritis, torn rotator cuff, and/or adhesive capsulitis, were studied. Patients with osteoarthritis showed significant pain and visual analog scale score improvement with both 3 and 5 glenohumeral injection regimens at both 7 and 26 weeks. However, this improvement was not maintained for every intermediary time point, and results are similar to previous studies investigating 3- and 5-injection regimens in the knee.¹²

Table 4. Study design for intra-articular injections of hyaluronic acid for osteoarthritis.^a

Study	Type	Patients, n	Follow-up, wk	Treatment Arm	Control Arm	Outcomes Measures
Noel ⁴³	Prospective	39	26	Hylan G-F 20	None	VAS
Silverstein ⁵⁰	Prospective	30	26	3 injections of Hylan G-F 20	None	VAS, UCLA, SST
Blaine ⁷	RCT	456	26	Sodium hyaluronate	Saline	VAS
Merolla ³⁸	Retrospective controlled	84	26	Hylan G-F 20	Methylprednisolone acetate	Constant-Murley, SPADI, satisfaction

^aRCT, randomized controlled trial; VAS, visual analog scale; UCLA, University of California–Los Angeles; SST, Simple Shoulder Test; SPADI, Shoulder Pain and Disability Index.

Table 5. Study design of hyaluronic acid injection for adhesive capsulitis.^a

Study	Type	Patients, n	Follow-up, wk	Treatment Arm	Control Arm	Outcomes measures
Itokazu ²⁷	Prospective	62	8	Sodium hyaluronate 25 mg (1/wk × 5)	None	ROM; pain at rest, motion, pressure
Calis ¹¹	RCT	95	12	Sodium hyaluronate	Triamcinolone acetate vs PT vs no treatment	Pain severity with passive ROM, functional considerations
Rovetta ⁴⁹	RCT	30	26	Sodium hyaluronate + triamcinolone	Triamcinolone + PT	ROM, pain
Tamai ⁵³	Prospective	11	6	Sodium hyaluronate	None	Coefficient of enhancement of synovium on MRI, JOA score

^aRCT, randomized controlled trial; ROM, range of motion; PT, physical therapy; MRI, magnetic resonance imaging; JOA, Japanese Orthopaedic Association shoulder score.

One study evaluated the efficacy of HA versus methylprednisolone acetate in arthritis in 84 patients at 1-, 3-, and 6-month intervals.³⁸ The HA group showed a significant pain reduction, improvement in Constant-Murley and Shoulder Pain and Disability Index scores, and satisfaction at all 3 follow-up times. In the corticosteroid group, improvements in pain, functional outcomes, and satisfaction were present only at 1 month. Outcomes were relative to the degree of arthritis and the presence of rotator cuff tears.

Adhesive Capsulitis

In a clinical study of viscosupplementation for adhesive capsulitis,²⁷ sodium hyaluronate was injected into the glenohumeral joint of 70 patients once per week over the course of 5 weeks. A global improvement rating demonstrated

that 51 of 62 patients (82.3%) were slightly improved or better and that 32 of 62 patients (51.6%) were moderately improved or better (Table 5). Pain at rest, motion, pressure, activities of daily living, and range of motion improved.²⁷


In a study of HA injection, triamcinolone acetate, or physical therapy modalities,¹¹ significant improvement was observed in pain, passive range of motion, and function on the 15th day after treatment and the third month for both HA treatment and steroid injections. Physical therapy alone demonstrated better pain reduction, passive range of motion, and function compared with both corticosteroid and HA injection.¹¹ While adhesive capsulitis can be treated with physical therapy, a combined HA and corticosteroids injection may offer a suitable alternative; patients that received both injections fared better functionally than those receiving corticosteroids only.⁴⁹ Researchers do not know why HA injections improve adhesive capsulitis outcomes. One study

suggests that clinical improvement may be related to a decrease in synovial inflammation or decreased synovial perfusion in the glenohumeral joint⁵³; another hypothesizes that the HA may decrease shoulder soft tissue retraction by influencing the volume of synovial fluid or regulating joint osmotic pressure.⁴⁹

CONCLUSIONS

There is little scientific support in the literature for the use of intra-articular corticosteroid injections to treat

glenohumeral arthritis.^{38,54} The use of intra-articular corticosteroids for adhesive capsulitis has inconsistent patient-oriented evidence but better literature support than for glenohumeral arthritis.^{4,8,18,24,48,57} Intra-articular HA injections for osteoarthritis and adhesive capsulitis show promise but lack any well-designed prospective trials to fully evaluate their effectiveness.^{7,11,27,38,43,49,50,53} While the use of corticosteroids and HA in the conservative management of osteoarthritis and adhesive capsulitis is widespread, its basis rests on limited evidence.



Clinical Recommendations

SORT: Strength of Recommendation Taxonomy
A: consistent, good-quality patient-oriented evidence
B: inconsistent or limited-quality patient-oriented evidence
C: consensus, disease-oriented evidence, usual practice, expert opinion, or case series

Clinical Recommendation	SORT Evidence Rating
Intra-articular corticosteroid injections may be helpful for reducing symptoms in glenohumeral arthritis. ^{38,54}	C
Intra-articular corticosteroid injections are helpful for reducing symptoms in adhesive capsulitis. ^{4,8,18,24,48,57}	B
Intra-articular HA injections may be helpful for reducing symptoms in glenohumeral arthritis and adhesive capsulitis. ^{7,11,27,38,43,49,50,53}	C

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