Defining the Role of Intra-Articular Injections in the Management of Knee Osteoarthritis Pain

June 23, 2012 • New York City

Education Partner:
Session 1: Defining the Role of Intra-Articular Injections in the Management of Knee Osteoarthritis Pain

Learning Objectives

1. Explain the pathophysiology of osteoarthritis pain (OA) of the knee and how current treatment options may affect various pain pathways and/or the potential for disease modification.
2. Consider individual patient and treatment characteristics (eg, comorbidities, stage of disease, level of pain, drug tolerability, previous response to treatment) when initiating a multimodal treatment plan for patients with knee OA.
3. Describe the individual clinical and patient characteristics that guide the selection of intraarticular corticosteroid and hyaluronic acid (HA) injection therapy.
4. Compare and contrast the clinical utility of intra-articular corticosteroids and/or HA injection therapy.

Faculty

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Assistant Professor of Family Medicine
UMDNJ-Robert Wood Johnson Medical School
Assistant Team Physician
Rutgers Athletics
New Brunswick, New Jersey

Jason P. Womack, MD, is an assistant professor of family medicine at the University of Medicine and Dentistry of New Jersey (UMDNJ)- Robert Wood Johnson Medical School. He serves as associate program director to the sports medicine fellowship and functions as the assistant team physician for Rutgers University Athletics. He has been on faculty in the department of family medicine since 2008.

He graduated from Rutgers University and attended medical school at UMDNJ - Robert Wood Johnson Medical School where he was a member of the Alpha Omega Alpha Medical Honors Society. Dr Womack pursued a residency in family medicine at Thomas Jefferson University Hospital in Philadelphia, Pennsylvania, and was elected chief resident. He returned to UMDNJ - Robert Wood Johnson for fellowship in sports medicine prior to being recruited as faculty.

Faculty Financial Disclosure Statement

The presenting faculty reports the following:
Dr Womack has no financial relationship to disclose.

Education Partner Financial Disclosure Statement

The content collaborators at Excellence in Medical Education (XME) report the following:
Jack Boyle, MD, and Ann Sherwood, PhD, have no financial relationships to disclose.

Acronym List

<table>
<thead>
<tr>
<th>Acronym</th>
<th>Definition</th>
<th>Acronym</th>
<th>Definition</th>
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<tbody>
<tr>
<td>AE</td>
<td>adverse events</td>
<td>OA</td>
<td>osteoarthritis</td>
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<tr>
<td>CHF</td>
<td>congestive heart failure</td>
<td>OARSI</td>
<td>Osteoarthritis Research Society</td>
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<tr>
<td>COX-2</td>
<td>cyclooxygenase inhibitor 2</td>
<td>PPI</td>
<td>proton pump inhibitor</td>
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<td>DM</td>
<td>diabetes mellitus</td>
<td>QoL</td>
<td>quality of life</td>
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<tr>
<td>GAIT</td>
<td>Glucosamine HCl/Chondroitin</td>
<td>SF</td>
<td>synovial fluid</td>
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<td></td>
<td>Arthritis Intervention Trial</td>
<td>SSRIs</td>
<td>selective serotonin reuptake inhibitors</td>
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<td>HA</td>
<td>hyaluronic acid</td>
<td>TCAs</td>
<td>tricyclic antidepressants</td>
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<td>MAOIs</td>
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<td>NSAIDs</td>
<td>nonsteroidal antiinflammatory drugs</td>
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<td>Universities Arthritis</td>
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Suggested Reading List


Defining the Role of Intra-articular Injections in the Management of Knee Osteoarthritis Pain

Jason P. Womack, MD
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Drug List

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<td>Glucosamine chondroitin</td>
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<td>HMM hyaluronan</td>
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<td>Hyalgan®</td>
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<td>Sodium hyaluronate</td>
<td>Euflexa®</td>
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<td>Tramadol</td>
<td>Ultram®</td>
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<tr>
<td>Tramadol citrate</td>
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Learning Objectives

After completing this exercise, participants will be able to:
- Explain the pathophysiology of osteoarthritis (OA) of the knee and how current treatment options may affect various pain pathways and/or the potential for disease modification
- Consider individual patient and treatment characteristics (eg, comorbidities, stage of disease, level of pain, drug tolerability, previous response to treatment) when initiating a multimodal treatment plan for patients with knee OA
- Describe the individual clinical and patient characteristics that guide the selection of intra-articular (IA) corticosteroid and hyaluronic acid (HA) injection therapy
- Compare and contrast the clinical utility of IA corticosteroids and/or HA injection therapy

Pretest Question 1

How often do you ask your obese patients about knee pain?

1. All of the time
2. Most of the time
3. Usually
4. Sometimes
5. Occasionally
6. Never

Pretest Question 2

In a patient with OA of the knee as well as diabetes and cardiovascular risk factors in whom acetaminophen has been ineffective, which therapeutic options would you consider? (Check all that apply.)

1. Oral NSAIDs
2. Increased acetaminophen dose
3. Topical NSAIDs/capsaicin
4. Glucosamine chondroitin
5. IA steroids
6. IA hyaluronate

NSAIDs = nonsteroidal anti-inflammatory drugs
Which of the following findings in a 45-year-old female patient with knee pain is suggestive of OA? (Check all that apply.)

1. Patient height is 5’5”, and she has a BMI of 26 kg/m²
2. She reports severe morning stiffness in both knees lasting 90 minutes or more
3. She reports that her knee pain is exacerbated by going up and down stairs, and that her knees become stiff after sitting for a prolonged time
4. Physical examination reveals a suspected effusion in the right knee

Which of the following findings in a 45-year-old female patient with knee pain is suggestive of OA? (Check all that apply.)

1. Patient height is 5’5”, and she has a BMI of 26 kg/m²
2. She reports severe morning stiffness in both knees lasting 90 minutes or more
3. She reports that her knee pain is exacerbated by going up and down stairs, and that her knees become stiff after sitting for a prolonged time
4. Physical examination reveals a suspected effusion in the right knee

Pretest Question 3

Two days ago, you performed a right-knee IA HA injection for a 48-year-old man with OA—the second in a planned series of IA injections. Your patient returns today with a slightly erythematous right knee that is tender and swollen. He denies constitutional symptoms. Your next course of action is to:

1. Inform the patient that he is having an allergic reaction to the HA injection
2. Inform the patient that the effusion will subside but that future HA injections are contraindicated
3. Aspirate the effusion and send to laboratory to evaluate for infection or crystaline arthropathy
4. Initiate antibiotic prophylaxis

Pretest Question 4

Please indicate your level of agreement with the following statement: If a patient with OA of the knee requires a HA injection, I will refer him/her to an orthopedist.

1. Strongly agree
2. Agree
3. Undecided
4. Disagree
5. Strongly disagree

Program Overview

- Epidemiology, risk factors, impact of disease
- Pathogenesis of OA
  - Stages of progression
  - Rheology of synovial fluid (SF)
  - Pain pathways
- Treatment
  - Goals of treatment
  - Multimodal approach to management of OA
- Benefits and risks of pharmacologic therapy
- IA knee joint injections: practice considerations
  - Injection technique: video

OA—Often Overlooked as a Serious Chronic Disease

- Approximately 27 million Americans have OA
  - 13.9% of adults age ≥25 years
  - 33.6% of those age ≥65 years
- Knee OA
  - 6.1% of all adults age ≥30 years
  - 12.1% (4.3 million) of adults age ≥60 years
- 11% of adults with knee OA need help with personal care, and 14% require help with routine needs

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OA Is No Longer a Disease of Old Age

- Chronic arthropathy
  - Disruption of joint cartilage
  - Abnormal SF
  - Progressive loss of joint function
- More common in women
- Common in the fifth or sixth decades
- Increasing prevalence in younger patients
  - Obesity
  - Genetics
  - Trauma

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- Chronic arthropathy
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Patients with Arthritis Are 54% (range, 49.2% to 60.5%) More Likely to Be Obese*

Patients with Arthritis are 54% (range, 49.2% to 60.5%) more likely to be obese.*

US Prevalence of Obesity in Individuals with and without Arthritis

Behavioral Risk Factor Surveillance System

* BMI (weight [kg] / height [m]^2) ≥ 30.0.

Image reproduced with permission from Centers for Disease Control and Prevention (CDC).


OA Is Associated with the Metabolic Syndrome*, Especially in Younger Individuals

Analysis of National Health and Nutrition Examination Survey III Data

OA correlates with MetS and each of the MetS components, especially in younger individuals

Prevalence of MetS

<table>
<thead>
<tr>
<th>Age</th>
<th>OA</th>
<th>No OA</th>
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<tr>
<td>18-64 y</td>
<td>65%</td>
<td>21%</td>
<td>&lt; .001</td>
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<tr>
<td>≥ 65 y</td>
<td>54%</td>
<td>45%</td>
<td>&lt; .045</td>
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</table>

* Metabolic syndrome (MetS) is defined as ≥ 3 of 5 cardiovascular risk factors: abdominal obesity, high triglycerides levels, low high-density lipoprotein cholesterol levels, hypertension, and hyperglycemia.


OA Symptoms Increase Sharply with Radiographic Progression

Women report greater pain and loss of function than men at all Kellgren-Lawrence (K/L) grades

OA Results from Biochemical and Physical Causes

- Multiple biochemical and physical causes
  - Proinflammatory mediators are elevated
  - Inflammatory and proliferative changes in synovial compartments
  - Changes in SF elasticity and viscosity
  - Altered chondrocyte metabolism
  - Increased protease production

Rheologic Properties of SF Are Changed in OA

- Rheologic properties, such as viscoelasticity, determine how matter deforms and flows in response to force
- SF interacts with articular cartilage to create a low-friction bearing at the joint
- HA, a glucosaminoglycan, is the major determinant of SF viscoelastic properties
- In OA, HA molecular weight and concentration are decreased, as are HA intermolecular interactions
- SF of lower viscoelasticity results


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Central and Peripheral Pain Pathways in OA


Presentation and Diagnosis of OA of the Knee

- Typical presentation
  - Pain with weight-bearing activities
  - Morning stiffness usually <30 minutes
  - Stiffness after prolonged sitting
  - Pseudo-instability
- Examination
  - Alignment
  - Gait
  - Core stability
  - ROM of hip and knee
  - Joint effusion, tenderness, laxity

Importance of Weight-bearing X-rays

Pain does not always correlate with Kellgren-Lawrence (K/L) grade

Images provided courtesy of Dr. Alfred Cianflocco.

Differential Diagnosis

- Chronic inflammatory arthritis, including RA
- Gout or pseudo-gout
- Hip arthritis
- Chondromalacia patellae (anterior knee pain)
- Anserine bursitis
- Insufficiency fracture
- Iliotibial band syndrome
- Joint tumors
- Meniscal tear


ROM = range of motion.

Diagnosis of OA of the Knee

- Physical examination and history are the most sensitive diagnostic tools
- Radiography
  - X-rays are the most important diagnostic tool for confirming OA
  - Weight-bearing knee x-rays
  - Radiographic changes do not correlate with severity of pain
- Magnetic resonance imaging
  - Generally, not a first-line tool for diagnosis of OA
  - May have role if mechanical symptoms present
- Laboratory tests
  - Blood test to rule out inflammatory arthritis or infection
  - SF analysis to rule out inflammatory arthritis or infection


The Golfer

- A 45-year-old man who presents with chronic mild to moderate knee pain that limits his golf playing
- He is taking an antihypertensive, metformin, and a sulfonylurea.
- Physical examination: BMI, 27.3; height, 5’10”; weight, 190 lb
- Vital signs: heart rate: 75 bpm; blood pressure: 130/82 mmHg
  - Mild valgus deformity at the knees, flat feet
  - No effusion
  - Mild quadriceps atrophy
  - Unable to maintain a single leg stance, with his hip dropping into Trendelenburg
- Standing, weight-bearing radiographs show lateral compartment joint-space narrowing, particularly in the posteroanterior flexion film


Trendelenburg
Case Study—The Golfer

Patient has tried over-the-counter analgesics without adequate relief.

- What would the next step be?
  1. Prescribe a COX-2 inhibitor for a limited amount of time
  2. Prescribe tramadol
  3. Try orthotics with a medial wedge
  4. Try physical therapy
  5. Consider intraarticular injections with corticosteroids or HA?

COX-2 = cyclooxygenase 2.

Multimodal Therapy for OA

- OARSI guidelines state: optimal management requires combination of nonpharmacologic and pharmacologic modalities
  - Strength of recommendation*: 96%

OARSI = Osteoarthritis Research Society International.
* Strength of recommendation based on the rating (on a scale of 1 to 100) by guideline development group after assessment of the research evidence for efficacy, safety, and cost-effectiveness of each treatment proposed, and the clinical experience of the guideline committee members with patient behaviors, compliance, and adherence to the treatment in question and their expert knowledge of any logistic issues.

Tailoring Treatment of OA of the Knee

- Knee risk factors (obesity, adverse mechanical factors, physical activity)
- General risk factors (age, comorbidity, polypharmacy)
- Level of pain intensity and disability
- Signs of inflammation (eg, effusion)
- Location and degree of arthritis
- Patient’s lifestyle and responsibilities


Treatment Goals for OA

Primary
- Reduce pain
- Improve joint mobility
- Limit functional impairment

Secondary
- Slow disease progression
- Improve muscular strength
- Avoid falls
- Preserve independence
- Improve patient quality of life
- Minimize drug-related complications
- Minimize surgical complications
- Delay surgery


Components of Individualized, Multimodal OA Therapy

- Exercise
- Weight loss
- Physical therapy
- Patient education
- Nutraceuticals
- Topical agents
- Analgesics
- NSAIDs
- Corticosteroid injections
- Hyaluronate injections
- Surgery

Tailor treatment based on individual patient characteristics.

Considerations in Patients with Comorbidities

- Renal: avoid NSAIDs and/or COX-2 inhibitors; use acetaminophen
- GI: avoid NSAIDs, or use with a PPI
- Hypertension, or CHF: avoid or rarely use NSAIDS and/or COX-2 inhibitors
- DM: Monitor blood glucose and A1C levels with IA steroids or long-term duloxetine; consider HA injections

PPI = proton pump inhibitor; CHF = congestive heart failure; DM = diabetes mellitus.
Nonpharmacologic

- Patient education—self-management
- Physical therapy and exercise—muscle strengthening and aerobic
- Weight reduction
- Thermal modalities
- Acupuncture
- Transcutaneous electrical nerve stimulation unit
- Shoe insoles or wedges
- Knee braces
- Walking aids—cane, rolling walker


Acetaminophen—Evidence-based Update

- Consider acetaminophen up to 3 g/d as initial treatment of mild to moderate OA pain
- Recent evidence shows that acetaminophen:
  - Is less effective than NSAIDs in relieving OA pain, in short-term studies
  - Has no effect on stiffness or function in patients with symptomatic knee OA
  - Carries risk of hepatotoxicity, especially if ≥3 g/d
  - Most common cause of liver failure
  - Increasing evidence of upper GI effects with long-term use, especially high doses used in combination with NSAIDs


Limited Evidence that Glucosamine and Chondroitin Improve Knee OA Pain

- NIH-sponsored, placebo-controlled, double-blind, randomized, controlled trial of 1583 patients with knee OA (GAIT) – Glucosamine 1500 mg + chondroitin 1200 mg for up to 2 years
  - Primary endpoint showed no benefit
- Subgroup analysis found significant improvement in those with moderate to severe knee pain only
- 2010 meta-analysis of 10 trials totaling 3803 patients
  - Chondroitin and glucosamine, alone or in combination, showed no clinically relevant effect on joint pain or on joint-space narrowing
  - Estimated treatment effects in industry-independent trials were small or absent, and clinically irrelevant
- Rare reports of shellfish allergy and potential warfarin interaction


Pharmacologic and Injectable Treatment Options: Alone or in Combination

- Pharmacologic
  - Oral analgesics (acetaminophen, NSAIDs, tramadol, opioids)
  - Topical analgesics (NSAIDs, capsaicin, lidocaine)
  - Duloxetine
  - Nutraceuticals (glucosamine; chondroitin)
- Injectable
  - Corticosteroid injections
  - HA injections


Topical Analgesics

- NSAIDs (diclofenac gel, patch, solution)
  - Recommended in OARSI guidelines as adjunctive or alternative treatment to oral therapies
  - Provided pain relief similar to oral NSAIDs in a single head-to-head trial
  - Maximum pain relief occurs after the first week of treatment
  - Safe; side effects similar to those of placebo in short-term (≤4-week) study
- Capsaicin (cream, patch, solution)
  - Recommended in OARSI guidelines as adjunctive or alternative treatment to oral therapies
  - Associated with burning sensation for several days after start of treatment
  - Lidocaine patch
    - Off-label for OA, indicated for postherpetic neuralgia
    - Side effects are rare, mild, and mostly related to skin rash
  - Salicylates
    - Not recommended in OARSI guidelines


Oral NSAIDs

- Superior to acetaminophen for patients with moderate to severe OA pain
- Side effects should be considered for individual patients
  - GI bleeding
    - Risk increases in combination with aspirin or high-dose acetaminophen
    - A PPI or misoprostol can be coadministered for high-risk patients
  - Patients at high risk for renal toxicity may not be candidates for NSAIDs
- Cardiovascular and cerebrovascular risks
- NSAIDs can reduce the benefits of prophylactic low-dose aspirin
- ≈16,500 NSAID-related deaths each year

**COX-2 Inhibitors**

- Endoscopic evidence shows a lower incidence of GI ulcers than traditional, nonspecific NSAIDs.
- However, the FDA states:
  - Associated with increased risk of serious adverse cardiovascular events, including stroke and myocardial infarction.
  - The potential for similar risks should be considered for nonspecific NSAIDs until proven otherwise.
  - Short-term use to relieve acute pain, particularly at low doses, does not appear to increase risk.

FDA = US Food and Drug Administration.


**Tramadol**

- FDA-approved for moderate to severe chronic pain.
- Weak µ-opioid agonist and norepinephrine and serotonin reuptake inhibitor.
- Need to weigh benefits and risks of central nervous system effects.
- Side effects:
  - Dizziness, nausea, headache, drowsiness, constipation.
  - Risk of seizures in patients taking selective serotonin reuptake inhibitors (SSRIs), tricyclic antidepressants (TCAs), monoamine oxidase inhibitors (MAOIs), or other opioids.
  - Risk of serotonin syndrome in patients taking SSRIs, TCAs, MAOIs, and triptans.
- Some risk of abuse.

**Duloxetine**

- Serotonin-norepinephrine reuptake inhibitor.
- Indicated for management of chronic musculoskeletal pain due to chronic OA.
- Maximum recommended dose: 60 mg/d.
- Most common adverse events (AEs): nausea, fatigue, and constipation.
- May worsen glycemic control over time in some patients.
- Blood pressure should be monitored.
- Duloxetine’s superiority over placebo for treatment of osteoarthritis appears to be modest at best.

**Opioids**

- OARSI guidelines state that, for most patients, significant side effects outweigh the benefits of opioids.
- Small to moderate improvement in:
  - Pain.
  - Function.
- Significant AEs:
  - Side effects: nausea, constipation, dizziness, somnolence.
  - Dependence/addiction.
- Patients should be chosen carefully, monitored, and assessed frequently.

**Potential Limitations with IA Corticosteroids**

- Adverse events (AEs) with IA corticosteroid injections are rare; a number of studies have demonstrated that IA injections are not associated with serious AEs.
- Potential adverse effects include:
  - Postinjection flares of pain, crystal synovitis, hemarthrosis, joint infection, and steroid articular cartilage atrophy.
  - Systemic corticosteroid effects, such as aggravation of hypertension, DM, steroid flares or fluid retention.
  - Accurate placement of injections is essential to reduce risk of fat necrosis and para-articular tissue atrophy.
- Experts recommend caution regarding frequent use (<4 times/y).

**IA Corticosteroid Injections: Effective for Acute Flares of Knee OA**

- IA corticosteroid injections provide good short-term pain relief (1-4 weeks).
- Treatment may need to be repeated to maintain efficacy.
- Efficacy of pain relief diminished after 2 years of IA injections every 3 months.

**References:**

Candidates for Corticosteroid Injections
(speaker’s opinion)

<table>
<thead>
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<th>Indicated for the Treatment of Acute OA</th>
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<tbody>
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<td>Candidates</td>
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<tr>
<td>• Patients with acute flares with effusion that do not respond adequately to other treatment options</td>
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<tr>
<td>• Those wishing to avoid surgery</td>
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<tr>
<td>• Patients who cannot take NSAIDS or who are on multiple medications</td>
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HA Injections Are Effective Long-term Therapy for Knee OA

- Efficacy similar to systemic interventions and superior to placebo
- Works well across OA spectrum
- More benefit in earlier-grade OA
- May reduce consumption of oral analgesics
- More prolonged effect than IA corticosteroids—up to 40 weeks
- Compared with systemic interventions
  - More local reactions (joint swelling, worsening of effusion, hemarthrosis)
  - Small risk of allergic response
  - Fewer systemic AEs
- Discontinuation rates due to AEs similar to placebo

HA Injections: Potential Mechanisms of Action

- Evidence from animal and human studies suggests that hyaluronate injections reduce pain and may inhibit joint destruction
  - Mechanical effects
    - Increase shock absorption
    - Increase lubrication
    - Create barrier around nociceptors (pain receptors)
  - Metabolic effects
    - Induce endogenous HA production
    - Inhibit proinflammatory cytokines and prostaglandins
    - Stimulate chondrocyte growth and extracellular matrix protein synthesis
    - Inhibit metalloproteinase activity
  - Reduces loss of knee cartilage over 2 years

Clinical Management of Severe Acute Inflammatory Reactions

- Aspirate fluid
- Analyze aspirated fluid
  - Gram stain/culture, cell count + differential, crystals
  - Observe for fever, return of pain/swelling
- Administer IA corticosteroid if no infection
- May resume HA injections when effusion resolves

Low Rate of Local Hypersensitivity Reactions

- Rate of local AEs are low (<1%) Similar to saline or corticosteroid injections
- Related to number of injections and severity of OA
- Most flare reactions occur within 24-48 hours
  - Self-limiting and often resolve spontaneously
  - The reaction is not anaphylactic
  - Patients recover well and benefit from procedure
  - Occurrence does not preclude patients from continuing with future courses of HA
  - More likely with inaccurate needle placement

Progressive Improvement with HA Injections over 40 Months

AMELIA (OsteoArthritis Modifying Effects of Long-term Intra-articular Adant) Study
Patients received 4 cycles of 5 IA HA or placebo injections

- N = 306
- N = 306

<table>
<thead>
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Hyaluronate Injections May Delay the Decision for Knee Replacement Surgery

- Patients who achieve reasonable pain levels, and are able to function, may choose to defer surgery
- Two retrospective analyses assessed rates of total knee replacement (TKR) in patients treated with hyaluronate injections
  - Retrospective analysis of 1 site
    - 1187 knees evaluated (OA grade 4)
    - Incidence of TKR was 19%
    - Median time to TKR: 1.8 years
    - 75% of knees—no TKR by 3.8 years
  - Retrospective analysis of 5 sites
    - 303 knees evaluated
    - Incidence of TKR was 7.6%
    - Mean time to TKR: 1.99 years

Waddell DD, Bricker DC. J Manag Care Pharm. 2007;13(2):113-121.

Candidates for Hyaluronate Injections (speaker’s opinion)

- Elderly patients with mild to severe OA of the knee
- Younger patients with mild to moderate OA of the knee
- Those wishing to delay knee surgery

Consider

- Patients with comorbidities who are taking multiple medications (eg, CHF, diabetes)
- Patients who cannot take NSAIDs (GI or renal disease, unstable hypertension)
- In whom other treatments may be contraindicated
- Patients who are too young for TKR
- Patients who have a medical contraindication for TKR

* Not for patients with severe joint deformity or infectious arthritis.

The Golfer, Part 2

The patient was prescribed tramadol for acute flares, a medial wedge, and physical therapy (PT). At his 8-week visit, he had gained 5 lb. He reported that he had not played golf in 2 months and had stopped PT because of the pain.

- What would you do next?
  1. Increase the tramadol dose?
  2. Prescribe duloxetine?
  3. Replace medial wedge with unloader brace?
  4. Consider injections with IA HA?

How Often Do You Perform IA Injections?

1. 1-3 times per month
2. 4-6 times per month
3. >7 times per month
4. I do not perform IA injections

HA Injections

<table>
<thead>
<tr>
<th>HA</th>
<th>MW [million Daltons]</th>
<th>Elasticity</th>
<th>Viscosity</th>
<th>Cross-linked</th>
<th>Source</th>
<th>Injections per cycle</th>
</tr>
</thead>
<tbody>
<tr>
<td>Healthy, young</td>
<td>60</td>
<td>157</td>
<td>2800</td>
<td>Not applicable</td>
<td>Asian</td>
<td>2.5-7.5 mg (or 1X 48-mg)</td>
</tr>
<tr>
<td>Synovial fluid</td>
<td>1.9</td>
<td>1.9</td>
<td>1.4</td>
<td>Not applicable</td>
<td>Asian</td>
<td>2 or 3</td>
</tr>
<tr>
<td>Hylan G-F 20</td>
<td>0</td>
<td>111</td>
<td>25</td>
<td>Not applicable</td>
<td>Asian</td>
<td>2.5-7.5 mg (or 1X 48-mg)</td>
</tr>
<tr>
<td>Sodium hyaluronate</td>
<td>0.5-1.7</td>
<td>0.6</td>
<td>2</td>
<td>No</td>
<td>Asian</td>
<td>2</td>
</tr>
<tr>
<td>Sodium hyaluronate</td>
<td>0.8-1.2</td>
<td>9</td>
<td>15</td>
<td>No</td>
<td>Asian</td>
<td>2 or 3</td>
</tr>
<tr>
<td>High molecular weight hyaluronate (60 mg)</td>
<td>1-2.9</td>
<td>60</td>
<td>46</td>
<td>No</td>
<td>Asian</td>
<td>3-4</td>
</tr>
<tr>
<td>Sodium hyaluronate</td>
<td>2.4-3.6</td>
<td>50</td>
<td>37</td>
<td>No</td>
<td>Non-avian</td>
<td>3 or 5</td>
</tr>
</tbody>
</table>

MW, molecular weight
†As in 18-27-year-olds.
§Non-avian product derived from a non-hemolytic strain of streptococcus

Common Approaches to IA Knee Injection

- Common approaches for injecting the knee include
  - Anterolateral (flexed knee)
  - Anteromedial (flexed knee)
  - Supernatilateral/lateral suprapatellar (straight knee)
  - Supernatilateral/medial suprapatellar (straight knee)
  - Lateral mid-patellar
  - Medial mid-patellar
**Selecting an Injection Approach**

- Lateral approach is superior to either anteromedial or anterolateral approaches (91% vs 75% and 71%, respectively).

**Identify and Mark the Injection Site**

- Superolateral approach
  - Palpate superolateral edge of patella with patient supine

**Prepare the Injection Site**

- Sterilization technique
  - Swab area with a povidone iodine preparation 3 times and let dry
- Local anesthetic options
  - Lidocaine
  - Ethyl chloride spray

**Aspiration**

- If effusion is present, aspiration is required to avoid diluting agent to be injected
- Insert needle (1½”;18-G needle with a 10-cc to 30-cc syringe) and begin aspiration
- If needle is accurately placed, the syringe should fill with fluid
- Compression of the opposite side of the joint or the patella may aid in arthrocentesis

**Injection**

- The same needle can be used for aspiration and injection
- If only injecting, use:
  - 22-G needle for corticosteroids
  - 20- to 22-G needle for HA (depending on product used)

**Injection Video**

Post-injection Care: Setting Patient Expectations and Managing Side Effects

• Avoid strenuous activity for 1 to 2 days after injection
• Mild pain or swelling at the injection site may occur
  – If it occurs, recommend ice, NSAID, rest, and elevation
• If significant pain or swelling occurs:
  – Joint aspiration
    • Send aspirate to laboratory to rule out joint infection
  – Crystal analysis
  – May provide IA corticosteroid to decrease pain and inflammation following HA injection

Surgical Consultation*

• Those with symptoms causing substantial impact on patient’s quality of life that are refractory to treatment
• Refer before prolonged/established functional limitation and severe pain
• Patient-specific factors (age, gender, smoking, obesity, and comorbidities) should not be barriers
• Decisions on referral thresholds should be based on discussions between the patient, family, the primary care physician, and the treatment team

* Speaker’s opinion.

Summary

• OA is a common, chronic disease that affects 27 million Americans
• Patients with obesity, cardiovascular risk factors, and diabetes are at higher risk for OA
• A multimodal approach, including nonpharmacologic, pharmacologic, and injectable therapies, should be considered
• Therapy decisions must also take into account the patient’s lifestyle, responsibilities, and comorbidities
• IA corticosteroids may provide relief for acute flares
• IA hyaluronic reduces long-term pain and may reduce cartilage loss over time

Guideline References


Posttest Question 1

As a result of this education, how often will you ask your obese patients about knee pain?

1. All of the time
2. Most of the time
3. Usually
4. Sometimes
5. Occasionally
6. Never
In a patient with OA of the knee as well as diabetes and cardiovascular risk factors in whom acetaminophen has been ineffective, which therapeutic options would you consider? (Check all that apply.)

1. Oral NSAIDs
2. Increased acetaminophen dose
3. Topical NSAIDs/capsaicin
4. Glucosamine chondroitin
5. IA steroid injections
6. IA HA injections

Which of the following findings in a 45-year-old female patient with c/o knee pain is suggestive of OA? (Check all that apply.)

1. Patient is 5’5” in height and has a BMI of 26 kg/m²
2. She reports severe morning stiffness in both knees lasting 90 minutes or more
3. She reports that her knee pain is exacerbated by going up and down stairs, and that her knees become stiff after sitting for a prolonged time
4. Physical examination reveals a suspected effusion in the right knee

As a result of this education, please indicate your level of agreement with the following statement: If a patient with OA of the knee requires a HA injection, I will refer him/her to an orthopedist.

1. Strongly agree
2. Agree
3. Undecided
4. Disagree
5. Strongly disagree

As a result of this education, how likely are you to seek additional education on administering intra-articular injections for OA knee pain?

1. Very Likely
2. Somewhat likely
3. Ambivalent
4. Not very likely
5. Will not seek additional education

Two days ago, you performed a right knee IA HA injection for a 48-year-old man with OA—the second in a planned series of IA injections. Your patient returns today with a slightly erythematous right knee that is tender and swollen. He denies constitutional symptoms. Your next course of action is to:

1. Inform the patient that he is having an allergic reaction to the HA injection
2. Inform the patient that the effusion will subside but that future HA injections are contraindicated
3. Aspirate the effusion and send to laboratory to evaluate for infection or crystalline arthropathy
4. Initiate antibiotic prophylaxis