Intra-articular Injections

Improving Mobility for the Management of Osteoarthritis

Wednesday, April 27, 2011 • 8:00–9:15 AM
Anaheim, California
Session 1: Intra-articular Injections: Improving Mobility for the Management of Osteoarthritis

Learning Objectives
1. Explain the pathophysiology of OA of the knee and the need for both disease modification and pain management.
2. Customize a multi-modal treatment plan to maximize mobility based upon stage of disease, comorbidities, drug tolerability and interactions, and response to treatment.
3. Identify patients in the primary care setting who may benefit from intra-articular injections of the knee and describe the benefits and risks associated with the administration of intra-articular injections for the treatment of OA of the knee.

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Dr Cianflocco obtained his undergraduate degree from John Carroll University and his medical degree from Wake Forrest University. He is primary care team physician for the Cleveland Cavaliers of the NBA and team physician for John Carroll University. He has also served as a medical consultant to the Cleveland Browns of the NFL, Cleveland Barons of the AHL, and the Winterhurst Figure Skating Program, as well as physician for the USFSA Championships, Senior PGA US Open Championship, and the Primus NHL Worldstars Tour.

Faculty Financial Disclosure Statements
The presenting faculty reported the following:

Dr Cianflocco is a consultant and speaker for Genzyme Corporation.

Education Partner Financial Disclosure Statements
The content collaborators at Excellence in Medical Education (XME) have reported that they have no relevant relationships to disclose.

Drug List

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<tr>
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<td>diclofenac topical</td>
<td>Pennsaid, Flector Patch</td>
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Off-Label
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<tr>
<td>glucosamine chondroitin</td>
<td>supplement</td>
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<tr>
<td>SAM-e</td>
<td>supplement</td>
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Suggested Reading List


Learning Objectives

- Explain the pathophysiology of osteoarthritis (OA) of the knee and the need for both disease modification and pain management
- Customize a multimodal treatment plan to maximize mobility based on stage of disease, comorbidities, drug tolerability and interactions, and response to treatment
- Identify patients in the primary care setting who may benefit from intra-articular injections of the knee and describe the benefits and risks associated with the administration of intra-articular injections for the treatment of OA of the knee

Pre-Test Question 1
How often do you order weight-bearing x-rays as part of the diagnostic work-up for OA of the knee?
1. Always
2. Most of the time
3. Sometimes
4. Rarely
5. Never

Pre-Test Question 2
Do you counsel your patients about taking over-the-counter (OTC) acetaminophen if you prescribe pain medication containing acetaminophen?
1. Always
2. Most of the time
3. Sometimes
4. Rarely
5. Never

Pre-Test Question 3
How confident are you at performing intra-articular injections in your practice?
1. Very Confident
2. Somewhat confident
3. Confident
4. Not Very Confident
5. Not At All Confident

Pre-Test Question 4
If you are treating an older patient (≥65 years) for OA of the knee with pain despite having used nonpharmacological and pharmacological interventions, are you more likely to:
1. Refer him/her for a surgical consultation?
2. Administer or refer him/her for intra-articular corticosteroid injections?
3. Administer or refer him/her for intra-articular viscosupplement injections?
Pre-Test Question 5

If you are treating a younger patient (<65 years) for OA of the knee with pain despite having used nonpharmacological and pharmacological interventions, are you more likely to:

1. Refer him/her for a surgical consultation?
2. Administer or refer him/her for intra-articular corticosteroid injections?
3. Administer or refer him/her for intra-articular viscosupplement injections?

OA—Definition

- Chronic arthropathy
  - Disruption of joint cartilage
  - Osteophyte formation
  - Abnormal synovial fluid
- Common in the fifth or sixth decades
- Posttraumatic in younger patients

OA: Scope of the Problem in the United States

- Affects ≈27 million Americans
  - 34% of the population ≥65 years
  - Common cause of disability; 25% of those with OA cannot perform major activities of daily living (ADL)
- Accounts for 25% of primary care visits
- Cost ≈$185 billion for healthcare annually

Risk Factors

**Modifiable**
- BMI ≥ 30
- Joint injury
- Malalignment
- Manual labor
- Tobacco Use

**Nonmodifiable**
- Genetic factors
- Black heritage
- Female gender
- Aging

Which of the following is associated with the development of OA of the knee? (Select all that apply.)

1. Inflammatory and proliferative changes in synovial compartment
2. Decreased protease activity
3. Changes in viscosity and elasticity of synovial fluid
4. Altered chondrocyte metabolism
5. Increased osteoclast activity
6. Decreased adipose cell metabolism
OA Pathophysiology

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

Pathogenic Factors in OA

- Obesity
- Anatomic abnormalities
- Microfractures and bony remodeling
- Loss of joint stability
- Trauma
  
  - Abnormal stresses
  - Abnormal cartilage

- Compromised cartilage
  
  - Aging
  - Genetic and metabolic diseases
  - Inflammation
  - Immune system activity

- Biophysical changes
  - Collagen network fracture
  - Proteoglycan unraveling

- Biochemical changes
  - Inhibitors reduced
  - Proteolytic enzymes increased

Presentation and Diagnosis of OA of the Knee

- Typical presentation
  - Pain with weight-bearing activities
  - Morning stiffness usually <30 minutes
  - Pseudo-instability

- Examination
  - Alignment
  - Gait
  - Core stability
  - ROM of hip and knee
  - Joint effusion, tenderness, laxity

Presentation and Diagnosis of OA of the Knee (cont’d)

- Radiography
  - X-rays are the most important tool in confirming OA
    - Weight-bearing knee x-rays, 4 views
    - Provides valuable corroborating evidence in cases of suspected OA
    - Radiographic changes do not correlate with severity of pain
  - MRI is generally not indicated for diagnosis of OA but may have a role if mechanical symptoms are present

- Laboratory tests
  - Blood test to rule out inflammatory arthropathy or infection
  - Synovial fluid analysis to rule out inflammatory arthritis, gout, pseudo-gout, or infection

Presentation and Diagnosis of OA of the Knee (cont’d)

- Diagnosis of OA of the knee is confirmed using 4 views

Importance of Weight-Bearing X-Rays

Images provided courtesy of Dr. Alfred Cianflocco.
**Differential Diagnosis**

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

**RA = rheumatoid arthritis.**


- Chronic inflammatory arthritis, including RA
- Gout or pseudo-gout
- Hip arthritis
- Chondromalacia patellae
- Anserine bursitis
- Insufficiency fracture
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**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 QOL
- Minimize Rx complications
  - NSAID: GI, renal, CV
  - Acetaminophen: hepatic toxicity
- Delay surgery

**SOL = quality of life; Rx = prescription; NSAIDs = nonsteroidal anti-inflammatory drugs; GI = gastrointestinal; CV = cardiovascular.**


- Reduce pain
- Improve joint mobility
- Limit functional impairment

**Secondary**

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**Multimodal Treatment Approach to Individualize Therapy**

- Weight loss
- Physical therapy
- Exercise
- Patient Education
- Assistive devices
- Acetaminophen
- NSAIDs
- Corticosteroid injections
- Viscosupplements
- Surgery
- Nutraceuticals
- Topical agents

**Tailor treatment based on individual patient characteristics**

**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
- Sign of inflammation—for example, effusion
- Location and degree of arthritis
- Patient’s lifestyle and responsibilities

**Considerations in Patients with Comorbidities**

- Renal: avoid NSAIDs; use acetaminophen
- GI: avoid NSAIDs, or use with a PPI
- Renal, hypertension, or CHF: use COX-2 inhibitors rarely or not at all
- DM: use injected corticosteroids cautiously; consider viscosupplements

**Optimal management requires combination of nonpharmacological and pharmacological modalities**

- Strength of Recommendation: 96%

**Abbreviations:** PPI = proton pump inhibitor; CHF = congestive heart failure; COX-2 = cyclooxygenase inhibitor 2; DM = diabetes mellitus.


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**Multimodal Therapy for OA**

- Optimal management requires combination of nonpharmacological and pharmacological modalities
  - Strength of Recommendation: 96%

Guidelines

- American College of Rheumatology (ACR) 2000
- The European League Against Rheumatism (EULAR) 2003
- National Centre for Health and Clinical Excellence (NICE) 2008
- American Society of Orthopaedic Surgeons. Treatment of Osteoarthritis of the Knee 2008
- Osteoarthritis Research Society International (OARSI) Recommendations 2010

Nonpharmacological Options: Alone or in Combination

- Patient education — self-management
- Telephone follow-up
- Exercise — strength and aerobic
- Weight reduction
- Thermal modalities
- Acupuncture
- TENS unit
- Shoe insoles — lateral wedge
- Knee bracing
- Walking aids — cane, rolling walker

Nonpharmacological Options: Alone or in Combination (cont’d)

- Bracing
  - Provides greater improvement in WOMAC scores than neoprene sleeve
- Lateral wedge
  - Insole use did not improve pain or function, but reduced NSAID use and increased compliance
  - 10-mm laterally wedged insole was well tolerated and provided a borderline-better response than valgus knee bracing in patients with Grade 1 OA
  - No reduction in varus malalignment with the use of a laterally wedged insole or a knee brace

Pharmacological Options: Alone or in Combination

- Acetaminophen
- Topical NSAIDs
- Topical capsaicin
- Glucosamine ± chondroitin
- S-adenosyl methionine (SAM-e)
- NSAIDs + PPI/H2 blockers/misoprostol
- COX-2 inhibitors
- Tramadol
- Opioids
- Inter-articular injections

Acetaminophen

- Recommended as first-line therapy
  - Symptom relief = NSAIDs
- Risk of hepatotoxicity, especially if >4 g/d
  - Most common cause of liver failure
- Combined with opioids in common analgesics
- January 2011: US Food and Drug Administration (FDA) asks manufacturers of prescription acetaminophen products to limit the maximum amount of acetaminophen in these products to 325 mg per tablet, capsule, or other dosage unit

Abbreviation: TENS = transcutaneous electrical nerve stimulation.
• Consider acetaminophen as initial and ongoing therapy of mild-moderate musculoskeletal pain
• NSAIDs and COX-2 inhibitors should be considered rarely, with caution
• Consider opioids in patients with moderate-severe pain, pain-related functional impairment, or diminished QOL due to pain

Topical NSAID—Diclofenac
• Available as
  – 1.3% patch—apply twice daily
  – 1.5% gel—apply 4 g four times daily
• Analgesia comparable with oral NSAIDs
  – Less effective in the first week
• Low plasma levels; peak at 10–20 hours
• Reduces pain and morning stiffness, and improves physical function
• Safe; side effects similar to placebo

Topical Capsaicin Cream
• Available OTC as 0.025%–0.075%; 3 to 4 times daily
• Contains a lipophilic alkaloid extracted from chili peppers, which depletes substance P
• 33% reduction in pain after 4 weeks, as measured by patient-rated VAS (number needed to treat = 4)
• Side effects in 44%
  – Burning pain
  – Stinging
  – Erythema

Glucosamine and Chondroitin
• Glucosamine—endogenous aminosugar
• Chondroitin—endogenous glycosaminoglycan
• Both are constituents of cartilage proteoglycans
• Not FDA-approved for OA
• Side-effect profiles are low

Recent Meta-analysis Found No Effect of Glucosamine, Chondroitin, or Both On OA of the Knee
• 2010 meta-analysis of 10 trials in 3803 patients
• Chondroitin, glucosamine, and their combination do not have a clinically relevant effect on perceived joint pain or on joint space narrowing
• Estimated differences between supplements and placebo were less pronounced, on average, in industry-independent trials, and estimated treatment effects in industry-independent trials were small or absent, and clinically irrelevant

Two Earlier Trials Suggest Efficacy in Moderate-to-severe Knee Pain
• GAIT1 and GUIDE2 trials were placebo-controlled, double-blind RCTs
• Involved 1583 patients with knee OA and 318 patients with moderate–severe knee OA, respectively
• Glucosamine + chondroitin treatment showed significant improvement in moderate–severe knee pain

Abbreviations: VAS = Visual analog scale.

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SAM-e (S-adenosyl methionine)

- SAM-e is widely used as a dietary supplement by US patients with OA, despite a 2002 systematic review that showed no improvement in pain for SAM-e when compared with placebo in patients with OA.

NSAID Toxicity

- Patients at risk of a GI event should be prescribed misoprostol or a PPI in conjunction with the NSAID.
- Patients at high risk for renal toxicity may not be candidates for NSAIDs.
- The hazard ratio for GI bleeds is much greater in patients treated with NSAIDs plus high-dose acetaminophen.

Oral NSAIDs

- Consider if pain not improved with acetaminophen, topical NSAIDs and glucosamine ± chondroitin.
- Pain relief superior to acetaminophen for moderate to severe pain.
- Evaluate for risk of upper GI and renal toxicity.
  - In elderly, 20%–30% of peptic ulcer hospitalizations and deaths are related to NSAID use.
  - ≈16,500 NSAID-related deaths each year.

COX-2 Inhibitors

- Endoscopic evidence shows a lower incidence of GI ulcers than traditional NSAIDs.
- However, the FDA states:
  - Associated with increased risk of serious adverse CV events, including stroke and myocardial infarction.
  - Short-term use to relieve acute pain, particularly at low doses, does not appear to increase risk.

Tramadol

- FDA-approved for moderate–severe pain.
- Centrally acting, weak μ-opioid agonist.
- Also inhibits reuptake of norepinephrine and serotonin.
- Second-step pain therapy.
- Some risk of abuse.
- Side effects: nausea, drowsiness, constipation.

Opioids

- Small-to-moderate improvement in:
  - Pain
  - Function
- Outweighed by significant adverse events:
  - Side effects: nausea, constipation, dizziness, somnolence
  - Dependence/addiction.

Case Study—The Caregiver Wife

- 68-year-old female with long-standing OA of the left knee
- Previously treated with acetaminophen, without adequate relief
- Trial of NSAIDs with GI side effects
- Adverse effects with tramadol/acetaminophen
- She is the main caregiver for her husband, who has early Alzheimer disease, and her goal is to continue caring for him as long as possible
- Physical examination: BMI, 21.6; height, 5’2”; weight, 118 lb
- Vital signs: HR: 86 bpm; BP: 125/75 mm Hg

Abbreviations: HR = heart rate; bpm = beats per minute; BP = blood pressure.

Intra-articular Corticosteroid Injections Are Effective Treatment for Knee OA

- Superior to placebo for treatment of OA
- Response is rapid but not sustained
- No major safety issues, but sample size restrictions preclude definitive comment
- Overall, the analyses support the use of intra-articular corticosteroids in treatment of knee OA

Intra-articular Corticosteroids

- Good short-term pain relief (1–4 weeks)
- Treatment may need to be repeated at frequent intervals to maintain efficacy
- Intra-articular corticosteroid injections every 3 months for 2 years showed efficacy for relief of pain after 1 year
  - This was not demonstrable after 2 years

Intra-articular Corticosteroids (cont’d)

- Potential adverse effects include
  - Postinjection flares of pain, crystal synovitis, hemarthrosis, joint sepsis, and steroid articular cartilage atrophy
  - Systemic corticosteroids effects such as fluid retention or aggravation of hypertension or DM
- Accurate placement of injections is essential to reduce risk of fat necrosis and para-articular tissue atrophy
- Experts recommend caution regarding frequent use
- Repeat injections >4 times per year are not recommended

Intra-articular Corticosteroids (cont’d)

- Intra-articular injections with corticosteroids should be considered particularly when patients have moderate-to-severe pain not responding satisfactorily to oral agents and in patients with effusions or other physical signs of local inflammation
Corticosteroids

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<tr>
<th>Corticosteroid Preparation</th>
<th>Equivalent Dose/Volume</th>
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<tr>
<td>Triamcinolone acetonide</td>
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<tr>
<td>Methylprednisolone acetate</td>
<td>40 mg/mL</td>
</tr>
<tr>
<td>Betamethasone Na3PO4</td>
<td>6 mg/mL</td>
</tr>
<tr>
<td>Dexamethasone mixture</td>
<td>8 mg/mL</td>
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Viscosupplementation Is Effective for the Treatment of Knee OA

- Hyaluronic acid (HA) is superior to placebo
- Clinical effect is moderate
- No major safety issues
- Comparable in efficacy with systemic interventions
  - Fewer systemic adverse events
- More prolonged effect than intra-articular corticosteroids, up to 26 weeks
- Analyses support use of HA in the treatment of knee OA
- Works well across OA spectrum
  - Better in earlier-grade OA

Viscosupplement Product Comparison

<table>
<thead>
<tr>
<th>Hylan G-F 20</th>
<th>Sodium Hyaluronate</th>
<th>High-molecular-weight Hyaluronan</th>
<th>1% Sodium Hyaluronate</th>
<th>Hylan G-F 20</th>
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<tbody>
<tr>
<td>Dose per injection</td>
<td>20 mg</td>
<td>25 mg</td>
<td>30 mg</td>
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<tr>
<td>Number of injections per treatment course</td>
<td>3</td>
<td>3</td>
<td>4</td>
<td>6</td>
</tr>
<tr>
<td>FDA-approved Duration of pain relief</td>
<td>3 injections: 3 mo</td>
<td>3 injections: 6 mo</td>
<td>6 mo</td>
<td>6 mo</td>
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<tr>
<td>Molecular weight (× 10^6 Da)</td>
<td>0.5-0.7</td>
<td>0.6-1.7</td>
<td>1.0-3.0</td>
<td>2.4-5.0</td>
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HA Shown to Delay TKR

- Retrospective single-center analysis
  - Candidates (100% grade 4 OA) had 3 hylan G-F 20 injections
  - 59% received ≤ 3 courses
  - Incidence of TKR was 19% (highest in patients aged 60–69 years)
  - 75% of knees—no TKR by 3.8 years
- Retrospective analysis of 5 sites
  - 303 knees evaluated; 835 injections of sodium hyaluronate
  - Pretreatment knee pain rated as moderate or severe
  - 23 knees resulted in TKR (7%)
  - 95% of knees—no TKR by 2 years

Low Rate of Hypersensitivity Reactions with HAs

- Hypersensitivity reactions are minimal: <1%
- Most flare reactions occur within 24–48 hours
- The reaction is not anaphylactic
  - This is likely a Type 4 reaction
- Usually occurs after the second or third injection
- Patients recover well and benefit from procedure
  - Occurrence does not preclude patients from continuing with future courses of HA

Clinical Management of Severe Acute Inflammatory Reactions

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

**Speaker’s opinion**

<table>
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<tr>
<th>Indicated for the treatment of pain in knee OA who have failed conservative nonpharmacologic therapy and simple analgesics (eg, acetaminophen)</th>
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<tbody>
<tr>
<td><strong>Candidates</strong></td>
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<tr>
<td>• Elderly patients across the OA spectrum</td>
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<tr>
<td>• Younger patients with mild-to-moderate OA of the knee</td>
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<td>• Those wishing to delay knee surgery</td>
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<td><strong>Consider</strong></td>
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<tr>
<td>• Patients with comorbidities taking multiple medications (eg, CHF, diabetes)</td>
</tr>
<tr>
<td>• Patients who cannot take NSAIDs (GI or renal disease; unstable hypertension)</td>
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<td>• Where other treatments may be contraindicated</td>
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<tr>
<td>• Patients who are too young for TKR</td>
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<tr>
<td>• Patients who have a medical contraindication for TKR</td>
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*Not for patients with severe joint deformity or infectious arthritis.*

How comfortable are you administering knee-joint injections?

1. Extremely comfortable
2. Very comfortable
3. Somewhat comfortable
4. Not very comfortable
5. Not at all comfortable

Benefits of Performing Intra-articular Injections

- Patients appreciate their primary care physician providing services that traditionally required referral to a specialist
- Patients avoid treatment delays
- Physician satisfaction increases when a variety of procedures are part of their practice
- Practice revenues can increase substantially

Common Approaches to Intra-articular Knee Injection

- Common approaches for injecting the knee include
  - Anterolateral (flexed knee)
  - Anteromedial (flexed knee)
  - Superolateral/lateral suprapatellar (straight knee)
  - Superomedial/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% versus 75% and 71%, respectively).

Identify and Mark the Injection Site

- **Superolateral Approach**
  - Palpate superolateral edge of patella with patient supine

Preparing 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–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 steroids
  - 20- to 22-G needle for viscosupplementation (depending on product used)

Postinjection 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 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 intra-articular corticosteroid to decrease pain and inflammation following viscosupplementation

Information on Knee Joint Injection/Workshops

- **American Academy of Family Physicians’ Scientific Assembly** (September 14–17, 2011; Orlando, Florida; $800–$1200)
- **National Procedures Institute** (regional locations throughout the US: $1000–$2000)
  - [http://www.npinstitute.com](http://www.npinstitute.com)
- **Product-specific workshops**
  - Contact manufacturers to schedule a workshop with a local representative
Surgical Consultation*

- Those with symptoms causing substantial impact on patient’s QOL 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, their primary care physician, and treatment team

* Speaker’s opinion.

Summary

- OA is a common chronic disease affecting 27 million Americans and accounts for 25% of primary care visits
- A multimodal approach including nonpharmacological modalities, such as weight loss, exercise, orthotics, pharmacological therapies such as analgesics, topical therapies, intra-articular corticosteroid injections, and viscosupplementation; and surgery, can benefit patients
- Intra-articular injections may allow you to offer more options to your patients as part of your practice
- Therapy decisions must also take into account the patient’s lifestyle, responsibilities, and comorbidities

Guideline References


Post-Test Question 1

How often do you order weight-bearing x-rays as part of the diagnostic workup for OA of the knee?

1. Always
2. Most of the time
3. Sometimes
4. Rarely
5. Never

Post-Test Question 2

Do you counsel your patients about taking over the counter acetaminophen if you prescribe pain medication containing acetaminophen?

1. Always
2. Most of the time
3. Sometimes
4. Rarely
5. Never

Post-Test Question 3

As a result of this education, how confident are you to perform intra-articular injections in your practice?

1. Very Confident
2. Somewhat confident
3. Confident
4. Rarely
5. Not Confident
Post-Test Question 4

Since having attended the Pri-Med program, if you are treating an older patient (≥65 years) for OA of the knee with pain despite having used nonpharmacological and pharmacological interventions, are you more likely to:

1. Refer him/her for a surgical consultation
2. Administer or refer him/her for intra-articular corticosteroid injections?
3. Administer or refer him/her for intra-articular viscosupplement injections?

Post-Test Question 5

Since having attended the Pri-Med program, if you are treating a younger patient (<65 years) for OA of the knee with pain despite having used nonpharmacological and pharmacological interventions, are you more likely to:

1. Refer him/her for a surgical consultation
2. Administer or refer him/her for intra-articular corticosteroid injections?
3. Administer or refer him/her for intra-articular viscosupplement injections?