Implementing AHRQ Effective Health Care Reviews

Helping Clinicians Make Better Treatment Choices

Gout: Diagnosis and Management

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The Agency for Healthcare Research and Quality (AHRQ) conducts the Effective Health Care Program as part of its mission to produce evidence to improve health care and to make sure the evidence is understood and used. A key clinical question based on the AHRQ Effective Health Care Program systematic review of the literature is presented, followed by an evidence-based answer based on the review. AHRQ's summary is accompanied by an interpretation by an *AFP* author that will help guide clinicians in making treatment decisions. For the full review, clinician summary, and consumer summary, go to https://www.effectivehealthcare.ahrq.gov/ehc/index.cfm/search-for-guides-reviews-and-reports/?pageAction=displayProduct&productID=2323.

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CME This clinical content conforms to AAFP criteria for continuing medical education (CME). See CME Quiz on page 634. Author disclosure: No relevant financial affiliations.

Key Clinical Issue

What is the accuracy of clinical decision tools and imaging for the diagnosis of gout in the primary care setting, and how effective are medications used to treat and prevent gout?

Evidence-Based Answer

The Diagnostic Rule and the Clinical Gout Diagnosis are two clinical decision tools that are 88% and 97% sensitive and 75% and 96% specific, respectively, in diagnosing gout when compared with monosodium urate crystal analysis. (Strength of Recommendation [SOR]: C, based on disease-oriented evidence.) Nonsteroidal anti-inflammatory drugs (NSAIDs), colchicine, and corticosteroids all effectively treat acute gout.

Clinical Bottom Line: Effectiveness of Treatments for Acute Gout Attack

Strategy	*Number of studies*	*Number of patients*	*Finding*	*SOE*
Colchicine	2 RCTs	229	Reduces pain compared with placebo	●●●
	1 RCT	184	A lower dose of colchicine is as effective as a higher dose but has fewer adverse effects	●●○
NSAIDs*	1 RCT and observational data	30 (in RCT)	Reduce pain	●●●
	16 RCTs	1,280	No differences among NSAIDs in effectiveness	●●○
Corticosteroids	4 RCTs	297	Reduce pain as much as NSAIDs	●●●
Animal-derived adrenocorticotropic hormone (not commonly used in clinical practice)	2 RCTs	107	Reduces pain as much as NSAIDs	●●○

Strength of evidence scale

High: ●●● There are consistent results from good-quality studies. Further research is highly unlikely to change the conclusions.

Moderate: ●●○ Findings are supported, but further research could change the conclusions.

Low: ●○○ There are very few studies, or existing studies are flawed.

Insufficient: ○○○ Research is either unavailable or does not permit estimation of a treatment effect.

NSAIDs = nonsteroidal anti-inflammatory drugs; RCT = randomized controlled trial; SOE = strength of evidence.

**—The known anti-inflammatory action of these agents was considered when assessing SOE.*

Adapted from the Agency for Healthcare Research and Quality, Effective Health Care Program. Diagnosis and management of gout: current state of the evidence. Clinician summary. Rockville, Md.: Agency for Healthcare Research and Quality; January 2017. https://www.effectivehealthcare.ahrq.gov/ehc/products/564/2323/gout-clinician-170131.pdf. Accessed July 26, 2017.

(SOR: A, based on consistent, good-quality patient-oriented evidence.) Urate-lowering therapy reduces serum urate levels and frequency of gout attacks at 12 months. (SOR: B, based on inconsistent or limited-quality patient-oriented evidence.) It does not lower the frequency of gout attacks during the first six months, likely because of the increased risk of gout attacks with the initiation of therapy. Prophylactic agents such as colchicine and NSAIDs should be used during the first six months of urate-lowering therapy. (SOR: A, based on consistent, good-quality patient-oriented evidence.)

Practice Pointers

This Agency for Healthcare Research and Quality (AHRQ) review assessed the accuracy of clinical decision tools and imaging to diagnose gout *(eTable A)*, as well as the treatment of gout in the primary care setting. Although the presence of monosodium urate crystals in joint aspirate remains the diagnostic standard, the Diagnostic Rule and the Clinical Gout Diagnosis decision tools predicted gout with 88% and 97% sensitivity and 75% and 96% specificity, respectively. The Clinical Gout Diagnosis tool is more accurate than the Diagnostic Rule and is based on a history of more than one attack of acute arthritis, development of maximal inflammation within one day, monoarthritis or oligoarthritis attack, redness over joints, painful or swollen first metatarsophalangeal joint, unilateral tarsal joint attack, tophi, and the presence of hyperuricemia. The sensitiv-

Clinical Bottom Line: Effectiveness of Strategies for Managing Hyperuricemia in Patients with Gout

Strategy	*Number of studies*	*Number of patients*	*Finding*	*SOE*
Management of hyperuricemia				
Urate-lowering therapy vs. placebo	4 RCTs	1,378	Reduces serum urate	●●●
	2 RCTs	1,129	Does not decrease the risk of acute gout attacks within the first 6 months	●●●
	1 open-label extension study	NR	Reduces the risk of acute gout attacks after 1 year	●●○
Febuxostat vs. allopurinol	1 RCT	2,269	No difference in serum urate-lowering effect	●●●
	1 systematic review	NR	No statistically significant differences in overall adverse events	●●●
	Subgroup of 1 RCT	2,269	Age and race do not affect the effectiveness of either drug	●○○
Prophylactic therapy with colchicine or NSAIDs	3 RCTs	4,103	Reduces the risk of acute gout attacks when initiating urate-lowering therapy	●●●
	1 RCT	190	Longer durations of prophylaxis (> 8 weeks) are more effective than a shorter duration when initiating urate-lowering therapy	●●○
	3 RCTs	4,103		
Monitoring treatment				
Treating to a specific target serum urate level	1 systematic review and 8 studies	NR	Reduces the risk of gout attacks	●○○

Strength of evidence scale

High: ●●● There are consistent results from good-quality studies. Further research is highly unlikely to change the conclusions.

Moderate: ●●○ Findings are supported, but further research could change the conclusions.

Low: ●○○ There are very few studies, or existing studies are flawed.

Insufficient: ○○○ Research is either unavailable or does not permit estimation of a treatment effect.

NR = not reported; NSAIDs = nonsteroidal anti-inflammatory drugs; RCT = randomized controlled trial; SOE = strength of evidence.

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ity and specificity of the clinical decision tools appear to be just as good as, if not better than, imaging without the added cost or risk. Dual-energy computed tomography was 85% to 100% sensitive and 83% to 92% specific for diagnosing gout. Ultrasonography was 74% sensitive and 88% specific.[1]

NSAIDs, colchicine, and corticosteroids were all effective in reducing the pain of acute gout. Low-dose colchicine (1.2 mg initially followed by 0.6 mg one hour later) reduces pain compared with placebo, and is as effective as a higher dosage (1.2 mg followed by 0.6 mg each hour for six hours) with fewer gastrointestinal adverse effects *(eTable B)*. Multiple NSAIDs (at variable dosages; a common comparator was indomethacin 50 mg three times daily) reduce pain with no differences among NSAIDs in terms of effectiveness. Corticosteroids (multiple agents and dosages, including a single 30-mg dose of prednisolone, prednisone 30-mg taper, and betamethasone, 7 mg intramuscularly once) also reduce pain. Allopurinol (100 to 300 mg daily) and febuxostat (20 to 240 mg daily) effectively lower serum urate levels but do not reduce the frequency of gout attacks in the first six months of therapy. The use of colchicine (0.6 mg twice daily) or NSAIDs in combination with urate-lowering therapy reduces the increased risk of gout attacks associated with initiation of urate-lowering therapy. After 12 months, urate-lowering therapy reduces the frequency of gout attacks. There is insufficient evidence to determine whether dietary and lifestyle changes are effective for managing gout; however, it is reasonable to recommend reducing dietary purines, red meat, shellfish, sugary drinks, and alcohol while encouraging weight loss and physical activity.[1]

The American College of Physicians (ACP) used this AHRQ review to develop diagnostic and treatment guidelines with concordant conclusions: moderate evidence to support the use of clinical decision tools; low-quality evidence for dual-energy computed tomography or ultrasonography to improve diagnostic accuracy; and strong evidence for NSAIDs, corticosteroids, and colchicine for acute gout attacks.[2,3] The ACP guidelines differ from those of the American College of Rheumatology, which recommend urate-lowering therapy to a serum urate level of less than 6.0 mg per dL (357 μmol per L).[4,5] However, based on the AHRQ findings, the ACP guideline states that the strength of evidence is low for a specific serum urate goal.[1,2] In the absence of stronger evidence supporting a specific urate goal, urate-lowering therapy may be titrated clinically to minimize gout flares.

EDITOR'S NOTE: *American Family Physician* SOR ratings are different from the AHRQ Strength of Evidence ratings.

The opinions and assertions contained herein are the private views of the authors and are not to be construed as official or as reflecting the views of the U.S. Army Medical Department or the U.S. Army Service at large.

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eTable A. Accuracy of Diagnostic Methods for Gout with Monosodium Urate Analysis as the Reference Standard

Diagnostic method	*Number of studies*	*Number of patients*	*Finding*	*SOE*
Clinical algorithm: the Diagnostic Rule	3	1,383	Sensitivity: 88% Specificity: 75%	●●○
Clinical algorithm: the Clinical Gout Diagnosis	3	1,383	Sensitivity: 97% Specificity: 96%	●●○
Dual-energy computed tomography	4	235	Sensitivity: 85% to 100% Specificity: 83% to 92%	●○○
Ultrasonography	8	633	Sensitivity: 74% Specificity: 88%	●○○

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SOE = strength of evidence.

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eTable B. Adverse Effects Associated with Pharmacologic Agents Used to Manage Gout

Intervention	*Adverse effects*
Colchicine	Gastrointestinal symptoms, fatigue, and headache
	Rare adverse effects include leukopenia, aplastic anemia, neuromuscular toxicity, and rhabdomyolysis
	Overdose in adults and children can be fatal
Nonsteroidal anti-inflammatory drugs	Dyspepsia, abdominal pain, headache, and reduced kidney function
	Rare adverse effects include bone marrow suppression, aseptic meningitis, and dermatologic adverse events
	Serious adverse effects include gastrointestinal perforations, ulcers, and increased risk of heart attack or stroke that can lead to death
Corticosteroids	Dysphoria and mood disorders, elevation in blood glucose, high blood pressure, weight gain, insomnia, and fluid retention may occur with short-term use
Allopurinol	Nausea, upset stomach, diarrhea, and elevated liver enzymes
	Rare but serious adverse effects include toxic epidermal necrolysis, Stevens-Johnson syndrome, bone marrow suppression, and DRESS syndrome
Febuxostat	Abdominal pain, diarrhea, musculoskeletal pain, liver function abnormalities, nausea, arthralgia, and rash
	Rare but serious adverse effects include cardiovascular thromboembolic events, hepatic failure, toxic epidermal necrolysis, Stevens-Johnson syndrome, and DRESS syndrome

DRESS = drug rash with eosinophilia systemic symptoms.

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