

A BRIEF OVERVIEW OF GOUT, HYPERURICEMIA, AND CHRONIC KIDNEY DISEASE



BACKGROUND

Gout has been steadily increasing worldwide, and is now the most common type of inflammatory arthropathy.¹ In the United States alone, its prevalence more than doubled between the 1960s and the 1990s^{2,3}, and it is now estimated at 3.9 percent of U.S. adults (8.3 million adults—6.1 million men and 2.2 million women).^{2,4} Hyperuricemia is also common, with a prevalence of 6-8 percent in healthy adults, and a prevalence of one in three adults who have uncontrolled hypertension and several cardiovascular risk factors.⁵ Concomitantly, the prevalence of chronic kidney disease (CKD) has been increasing, with estimates at 14 percent of adults in the United States,⁶ and 8-16 percent globally.⁷

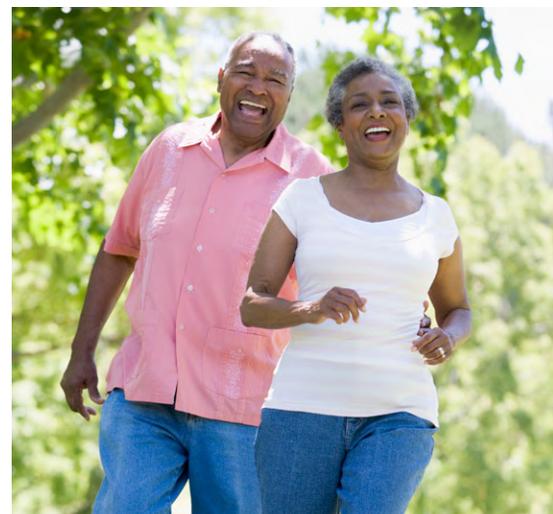
LOWERING SERUM URIC ACID TO TREAT GOUT IN THE SETTING OF CKD

PHARMACOLOGIC STRATEGIES

The 2012 American College of Rheumatology (ACR) Guidelines emphasize both non-pharmacologic and pharmacologic approaches for managing gout and lowering serum uric acid levels. The recommended serum uric acid level should be low enough to effectively improve and maintain the signs and symptoms of gout, a goal most often associated with a level of <6 mg/dL. The two first-line options for urate lowering therapy (ULT) are the xanthine oxidase inhibitors, febuxostat and allopurinol. Febuxostat does not require renal dose adjustment in mild to moderate CKD. Because insufficient evidence exists on its safety in severe CKD, no recommendation was issued for febuxostat in this setting. The starting dose for allopurinol should be no more than 100 mg/day in moderate to severe CKD, followed by gradual

upward titration of the maintenance dose, which can exceed 300 mg/day. Anti-inflammatory prophylaxis of acute gouty arthritis also involves the continuation of established pharmacologic ULT, without interruption, during an acute gout attack.⁸

The ACR recommends prophylaxis when initiating ULT because the rapid decrease in serum urate can often trigger gout flares. First-line options include low-dose colchicine (0.6 mg orally once or twice daily, with lower doses for moderate to severe CKD (eGFR of <60 mL/min/1.73 m²) and potential drug-drug interactions). Although low-dose non-steroidal anti-inflammatory drugs (NSAIDs) such as naproxen, 250 mg orally twice daily is recommended by the ACR, NSAIDs should generally be avoided in CKD. A stronger level of evidence exists for using colchicine.⁹



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NON-PHARMACOLOGIC STRATEGIES

Recognizing that improving the comorbidities for gout (e.g. hypertension, diabetes, and obesity) can also lead to decreased serum urate levels and gout flares, the ACR guidelines emphasize using non-pharmacologic interventions in all cases of gout.⁸ This approach is even more important in CKD because many gout medications can potentially be harmful to the kidneys, and therefore adjuvant methods of decreasing drug burden are helpful. Additionally, CKD shares the same comorbidities found in gout, including the metabolic syndrome and cardiovascular disease.^{1,10,11} In order to address these conditions, the ACR developed a comorbidity checklist to help guide patient education,

and to encourage individualized care through review of serum urate-elevating medications that could be eliminated or safely substituted, notably thiazide and loop diuretics, niacin, and cyclosporine and tacrolimus.^{1,9}

Specific diet recommendations from the ACR based on the strongest evidence include: limiting alcohol, particularly beer, as well as meat and seafood; a weaker recommendation was issued for avoiding foods and beverages that are high in fructose.^{8,12} Preventing dehydration has been found to be a simple and effective way of preventing gout attacks,¹³ and weight loss may be a meaningful intervention for decreasing serum urate levels in some patients.^{12,14} However, the ACR



also recognized that for a great number of patients with gout, diet and lifestyle changes alone are insufficient to achieve serum urate-lowering effects and/or gout attack prophylaxis.^{8,12}



CONCLUSION

As emphasized by both the ACR and the National Kidney Foundation, lifestyle and dietary modifications that ameliorate the features of gout and hyperuricemia, along with appropriate pharmacologic treatments for gout and uric acid nephrolithiasis, are the proven strategies for reducing the risk of developing or worsening CKD.^{8,15}

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