Treat to Target in Gout

By Abhijeet Danve, MD, FACP; and Tuhina Neogi, MD, PhD

Gout is the most common inflammatory arthritis affecting 42 million adults worldwide.[1] Despite the well understood pathophysiology and availability of effective medications, gout care remains suboptimal and adherence to therapy is poor. The central strategy in gout management is to reduce serum urate (sUA) to below the saturation threshold (6.8mg/dL= 408 μMol/L) to prevent monosodium urate crystallization, thereby reducing risk of gout flares and tophi. Because of this understanding of the biology of gout, a treat-to-target (T2T) strategy has been advocated by rheumatology societies, though this recommendation has not been accepted by all organizations.[2] A T2T strategy involves management of the index condition with frequent monitoring of disease activity while escalating treatment to achieve a pre-specified quantifiable therapeutic target, in contrast to using symptoms alone as a gauge. A T2T strategy is used in a number of chronic conditions including hypertension, diabetes, and rheumatoid arthritis.[3-5]

A criticism of T2T in gout has been whether sUA is an adequate marker of clinical disease manifestations of flare and tophi, but at least three randomized clinical trials (RCTs) to date have provided insights into the effects of lowering sUA to <6mg/dL (360 μMol/L) on clinically relevant outcomes.[6-8] A UK trial of nurse-led care that involved specific use of a T2T strategy with dose titration compared with usual care by general practitioners demonstrated lower sUA, which was accompanied by decreased severity and frequency of flares, reduction in tophi and improved medication adherence.[8] In a RCT carried out in participants with early gout, there was a greater proportion achieving sUA <6mg/dL (360 μMol/L) along with a greater decrease in overall flare incidence in the febuxostat arm compared with placebo.[7] Similarly, Sundy et al. demonstrated that use of pegloticase resulted in significantly more participants achieving sUA <6mg/dL (360 μMol/L), as well as a greater proportion with reduction in tophi and flares compared with placebo.[6] It is a fair concern that the specific threshold of <6mg/dL (360 μMol/L) has not been directly assessed in a RCT as being better than <6.8mg/dL (408 μMol/L) or <5mg/dL (300 μMol/L), for example. Nonetheless, these trials do provide support for lowering sUA to sufficiently below the saturation threshold to achieve improvements in the clinical outcomes of flares and tophi.

With consideration of these and other data in the comprehensive evidence report, the American College of Rheumatology (ACR) 2020 gout guidelines strongly recommended a T2T strategy with urate-lowering therapy (ULT) dose titration guided by serial sUA levels to achieve a target of <6 mg/dL (360 μMol/L). It also recommended that ULT titration should occur over a reasonable time frame to prevent treatment inertia.[9] The 2016 European League Against Rheumatism (EULAR) recommendations for the management of gout also supported use of a T2T strategy with a goal sUA of <6mg/dL (360 μMol/L).[10]

In summary, there is now high-quality data available combined with good understanding of gout's pathophysiology, and treatment guidelines to support T2T in gout. Thus, rather than practicing "reactive" health care, a proactive T2T approach can mitigate and prevent the long-term sequelae of inadequately managed gout.

Abhijeet Danve, MD, FACP
Assistant Professor of Medicine,
Yale School of Medicine
New Haven, Connecticut

Tuhina Neogi, MD, PhD
Professor of Medicine,
Boston University School of Medicine
Boston, Massachusetts

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