Latest recommendation for gout treat –To target

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Abstract

The treat-to-target concept has been applied successfully in several inflammatory rheumatic diseases. Gout is a chronic disease with a high burden of pain and inflammation. The pathogenesis of gout is strongly related to serum urate levels, gout may be an ideal disease for application of "treat-to-target" approach.

Keywords: Serum urate, Urate lowering therapy, Treat-to-target, Hyperuricaemia, Monosodium urate.

Patients with gout have not been treated optimally since ages[5] despite the availability of effective and safe urate lowering therapies. Traditional such therapies also include allopurinol, uricosurics (probenecid, benzbromarone) and new additions including flebuxostat, pegloticase and lesinurad. Re-learning the already available therapies for gout effectively, it is appropriate to practice evidence-based medicine and discard myths and wrong perceptions related to urate lowering therapies dosing and rare associated harms.

In this context, an expert group[1] has developed nine recommendations for gout management based on systemic literature review using standard methodology based on Oxford Center for Evidence-based Medicine system.

Aiming to achieve target serum uric acid, it is emphasized that it should be measured regularly in patients with gout so that urate lowering therapy dose adjustment can be guided. Highlight of these recommendations revolves round the goal that serum urate should be lowered and maintained at target serum uric acid level.

1. <6 mg/dL) (<360 μmoI/L) in all patients with gout (high-level evidence)
2. <5 mg/dL (<300 μmoI/L) in those with severe gout (including tophi or frequent attacks; expert opinion).

These recommendations and gout treatment guidelines[2-4] already support a treat-to-target tactic in gout with a goal of serum urate target of <6 mg/dL) (<360 μmoI/L) in all patients with gout and <5 mg/dL) (<300 μmoI/L) in patients with tophaceous or severe gout.

Why these targets

This serum urate target achievement is based on the saturation point for monosodium urate since achievement of target serum urate <6 mg/dL has been shown to lead to dissolution of crystals,[14] as well lower risk of gout flares, tophi and medical care costs.[15-18] A higher serum urate is associated with a higher risk of gout flares,[15-18] which present with severe pain and reduction of health-related quality of life.[19,20]

The nine latest recommendations[1] for gout management are:-

		LoE	GoR	SoR
1.	Serum urate must be measured regularly and urate-lowering therapy should be adjusted to attain the therapeutic target.	2	B	9.8±0.6
2.	A serum urate level <6 mg/dL (<360 μmoI/L) should be targeted and maintained in all patients with gout	1	A	9.5±0.9
3.	In patients with severe gout, such as those with tophi or frequent attacks, the target should be a serum urate level <5 mg/dL (<300 μmoI/L) until clinical remission is achieved	5	D	9.2±1.5
4.	Acute attacks should be treated promptly with anti-inflammatory medications, taking safety issues into consideration	5	D	9.9±0.5
5.	Prophylaxis against attacks should be initiated and continued for at least 6 months after starting urate-lowering therapy	5	D	8.3±1.7
6.	In all patients with gout, renal function should be assessed at the time of diagnosis and then monitored regularly	5	D	9.6±0.7
7.	Comorbidities associated with gout may influence therapy and outcomes and should be assessed regularly and managed	5	D	9.5±0.8
8.	Modifiable risk factors should be addressed primarily through patient education and support	5	D	9.2±1.5
9.	Information about gout and its management should be made readily available to patients by their healthcare professionals	5	D	9.7±0.7

SoR on a 0-10 scale with 0=no agreement aat all and 10=very strong agreement.
GoR, grade of recommendation; LoE, level of evidence; SoR, strength of recommendation.

Gout is caused by deposition of monosodium urate crystals within joints in the setting of chronic hyperuricaemia.[6] It affects 1%-2% of adults in developed countries and is the most common type of inflammatory arthritis worldwide. Epidemiological data are consistent with a rise in the prevalence and incidence of gout.[7,8] Nutrition and genetic polymorphisms of renal transporters of urate and other genes seem to be the main causal factors of primary gout. Gout and hyperuricaemia are associated with hypertension, diabetes mellitus, metabolic syndrome and renal and cardiovascular diseases.[6,9,10] There is a strong link between gout and increased risk of death from all causes and cardiovascular diseases.[11] The economic burden of gout is considerable.[12]

Gout is a common clinical problem encountered by both general and specialist clinicians. The key principles of gout management include establishing a definitive diagnosis, treating acute attacks promptly and using urate-lowering therapies appropriately to dissolve monosodium urate crystals to eventually prevent further attacks and joint damage. When serum urate concentrations are lowered below the saturation point of monosodium urate, new crystal formation is prevented, existing crystals dissolve and gout can be cured. The 'gold standard' diagnostic test for gout remains the identification of monosodium urate crystals by polarized light microscopy in synovial fluid cells or in a tophus.[13]

In many areas of medicine, such as diabetes care or cardiology, clear therapeutic targets have been defined and the continuous effort to reach these targets is standard practice.[21-26] More recently, treatment targets have also been advocated for rheumatoid arthritis, spondyloarthritides including psoriatic arthritis and systemic lupus erythematosus, namely remission or low disease activity.[27,28] These recommendations have been based on insights gained from systematic literature reviews of clinical trials.[29,30] The successful application of a treat-to-target strategy in a rheumatologic disease was first reported in rheumatoid arthritis and subsequently in psoriatic arthritis.[31,32]

Potential harms would also be an issue if we consider treating patients after their first gout attack, as per the updated European League Against Rheumatism gout recommendations[2] and the Swedish drug administration. If we become more aggressive in the treatment of gout at an early stage of the disease with a goal of preventing its future consequences, then we need to study benefit/harms/cost balance of an aggressive approach compared with delaying the initiation of treatment with urate-lowering therapy.

The deposition of urate crystal in joints and tendons occurs very early during disease course in gout[33] and tophi are an important outcome in gout. Radiographic damage in rheumatoid arthritis becomes a matter of concern, similarly in gout treatment it is aimed that urate crystal deposits resolve by a treat-to-target approach[34] before they produce any radiological footprint.

Cadiovascular outcomes are more frequent in several inflammatory rheumatic conditions. Gout is no exception and frequently have cardiovascular and renal comorbidities.[35]

A different serum urate cut-off/target that is more specific for gender, race or underlying comorbidities may emerge in the future. With an improved understanding of multi-system effects of hyperuricaemia on heart and kidneys, evidence is emerging for a beneficial effect of urate-lowering therapy on cardiovascular and renal outcomes,[36-38] even in patients without definite gout. A symptomatic hyperuricaemia due to lack of evidence has prompted a treatment target similar to one recommended for gout. Additional non-musculoskeletal benefits of urate-lowering therapy are being investigated.[39,40] Till the time the knowledge gap is addressed regarding the moot question, whether reaching target serum urate will prevent gout flares and ameliorate the cardiovascular and renal outcomes, the latest nine recommendations will help us to treat gout to target.

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