

Targeting uric acid levels in treating gout

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Clinical question

To prevent gout recurrence, should we prescribe urate-lowering therapies (eg, allopurinol) to target uric acid levels?

Bottom line

Best evidence finds that increasing the dosage of allopurinol to achieve a serum urate target (eg, <360 µmol/L) does not reduce gout flares, pain, or function compared with standard allopurinol dosage. Febuxostat increases cardiovascular death and overall mortality and should not be used in most patients with gout.

Evidence

- One RCT followed 183 patients taking allopurinol (mean dose approximately 270 mg/d) for gout with persistently elevated serum urate levels (mean 430 µmol/L) and more than 3 flares in the past year.¹ Patients were randomized to either escalating allopurinol dose to achieve a target serum urate level (<360 µmol/L) or current allopurinol dose. After 12 months, results were as follows:
 - Mean daily allopurinol dose was 390 mg for the intervention group and 290 mg for the control group.
 - More than 1 gout flare occurred in 54% of the intervention group and 59% of controls (no statistical difference).
 - The intervention group achieved serum urate levels of less than 360 µmol/L more often than the control group (69% vs 32%).
 - No differences in tophi resolution, functional status, pain, serious adverse events, rash, or gastrointestinal complaints were found.
- A systematic review of 10 RCTs (N=6100) of urate-lowering therapies found no relationship between achieving a target serum urate level (<360 µmol/L) and gout flare.²
 - Cohort studies found having fewer gout flares was associated with longer use of urate-lowering therapies and serum urate levels of less than 360 µmol/L.

Context

- A recent guideline³ recommends “treat to target” for serum urate levels, while another guideline⁴ finds insufficient evidence to recommend treat to target.
- Febuxostat (vs allopurinol) increases the following:
 - The proportion of gout flares (at up to 1 year)⁵: 44% with febuxostat versus 38% with allopurinol (number needed to harm [NNH] of 19).
 - Cardiovascular death⁶: 4.3% with febuxostat versus 3.2% with allopurinol (NNH=91).
 - All-cause mortality⁶: 7.8% with febuxostat versus 6.4% with allopurinol (NNH=72).
 - Health Canada warns against febuxostat use in patients with cardiovascular disease.⁷
- Starting allopurinol and colchicine concurrently during a gout flare does not prolong or worsen the flare.⁸

Implementation

Adherence to urate-lowering therapy ranges from approximately 50% to 87% after 1 year.⁹ When compared to other common chronic medical conditions, gout might have the lowest medication adherence.¹⁰ Using health care supports such as nurses or pharmacists in gout management (including education and prophylactic medications) might increase adherence and reduce gout flares.¹¹ In patients starting allopurinol, adding colchicine for the first 3 months helps decrease initial flares.¹²

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Competing interests
None declared

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