Who let the Gout Out? Targeting Uric Acid Levels in Treating Gout

Clinical Question: To prevent gout recurrence, should we dose urate lowering therapies (like allopurinol) to target uric acid levels?

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

Evidence:

- One randomized, controlled trial (RCT) evaluated 183 patients on allopurinol (mean dose ~270 mg/day) for gout with persistently elevated serum urate levels (mean 430 μmol/L) and more than 3 flares in the past year. Randomized to escalating allopurinol dose to achieve a target serum urate of <360 μmol/L or continue their current allopurinol dose. After 12 months:
  - Mean daily allopurinol dose: 390 mg intervention, 290 mg control.
  - ≥ 1 gout flare: 54% intervention, 59% control: not statically different.
  - Intervention group achieved serum urate <360 μmol/L more often: 69% versus 32%.
  - Tophi resolution, functional status, pain: no difference.
  - No difference in serious adverse events, rash, or gastrointestinal complaints.
- One systematic review found:
  - 10 RCTs (6100 patients) of urate lowering therapies reported no relationship between patients achieving serum urate <360 μmol/L and gout flare risk.
  - Cohort studies of urate lowering therapies found an association between fewer gout flares and:
    - An increased length of time a patient is on urate lowering therapies.
    - Serum urate levels <360 μmol/L.
Context:
- Most guidelines³ recommend a “treat to target” strategy for serum urate levels, while a recent guideline⁴ concludes insufficient evidence to recommend “treat to target.”
- Compared to allopurinol, febuxostat increases:
  - The proportion of gout flares (at up to one year):⁵ 44% febuxostat versus 38% allopurinol; number needed to harm (NNH)=19.
  - Cardiovascular death:⁶ 4.3% versus 3.2% allopurinol, NNH=91.
  - All-cause mortality:⁶ 7.8% versus 6.4% 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 flare.⁸

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Disclosures:
Authors do not have any conflicts of interest to declare.

References: