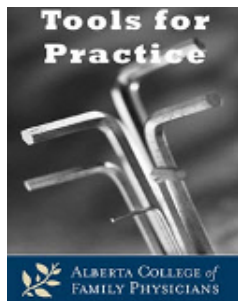


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May 19, 2020



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 $\mu\text{mol/L}$) 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 $\mu\text{mol/L}$) and more than 3 flares in the past year.¹ Randomized to escalating allopurinol dose to achieve a target serum urate of <360 $\mu\text{mol/L}$ 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 $\mu\text{mol/L}$ 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 $\mu\text{mol/L}$ and gout flare risk.²
 - 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 $\mu\text{mol/L}$.

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:

1. Stamp LK, Chapman PT, Barclay ML, *et al.* Ann Rheum Dis. 2017 Sep; 76(9):1522-1528.
2. Stamp L, Morillon MB, Taylor WJ, *et al.* Semin Arthritis Rheum. 2018 Oct; 48(2):293-301.
3. Li Q, Li X, Wang J, *et al.* BMJ open. 2019; 9(8):e026677.
4. Qaseem A, Harris RP, Forciea MA, *et al.* Ann Intern Med. 2017 Jan 3; 166(1):58-68.
5. Faruque LI, Ehteshami-Afshar A, Wiebe N, *et al.* Semin Arthritis Rheum. 2013; 43:367-75.
6. White WB, Saag KG, Becker MA, *et al.* N Engl J Med. 2018 Mar 29; 378(13):1200-1210.
7. Health Canada. Available at: <https://healthycanadians.gc.ca/recall-alert-rappel-avis/hc-sc/2019/71511a-eng.php>. Last Accessed: March 26, 2020.
8. Hill EM, Sky K, Sit M, *et al.* J Clin Rheumatol. 2015 Apr; 21(3):120-5.