**Gout**

**Update Pearls for Acute and Chronic Management**

**October 2009**

**Recent Guidelines:**
- EULAR European League Against Rheumatism [http://ard.bmj.com/cgi/reprint/65/10/1301](http://ard.bmj.com/cgi/reprint/65/10/1301)
- Management Guidelines 2006 [EULAR](http://ard.bmj.com/cgi/reprint/65/10/1312)

**Review Articles:**
- JAMA [http://jama.ama-assn.org/content/309/1/266](http://jama.ama-assn.org/content/309/1/266)
- BMJ [http://www.bmj.com/content/336/7639/329](http://www.bmj.com/content/336/7639/329)

**Patient Resources:**

**RxFiles Related:**
- [Gout Chart](http://www.rxfiles.ca/rxfiles/uploads/document/extra/RxFiles_Gout.pdf)

**General Overview**
- Gout is the most common form of inflammatory joint disease in men over the age of 40. Diagnosis is usually made on presentation of acute attack – i.e. “typical” attacks, or presence of tophi. (Definitive diagnosis requires the presence of uric acid crystals in the synovial fluid upon joint aspiration).
- Rule out: arthritic (septic, rheumatoid, osteo) & pseudogout

**Which NSAID to use for gout?**
- Many studies have shown that different NSAIDs provide similar benefits; any NSAID could be a reasonable choice if no contraindication.
- Indomethacin commonly used historically, however other NSAIDs equally effective with less side effects. Consider naproxen, ibuprofen or celecoxib.

**When should you avoid NSAID use?**
- **Contraindications (CI):**
  - Chronic kidney disease (CKD) Stage ≥IV prostaglandins are required to maintain renal perfusion.
  - Heart failure (HF): can cause exacerbations, salt & fluid retention
- **Precautions:**
  - those with a gastrointestinal (GI) history of ulcer or bleed; may consider use if also GI protection (e.g. PPI)
  - elderly & indomethacin: ↑ CNR risks, e.g. headache, confusion
  - those at high cardiovascular (CV) risk
- **Systematic Reviews: CV Risk with NSAIDs**
  - Observational studies 21:
    - Risk = naproxen < ibuprofen < indomethacin < diclofenac
  - RCTs 26:
    - Risk = naproxen < ibuprofen < indomethacin < diclofenac = Coxibs
- **Drug interactions (DI):** NSAIDs have MANY DIs.
  - e.g. Lithium disrupt serum levels: ACEIs/ARBs ↑K, warfarin, increased bleeding risks: ASA & ibuprofen, displacement of ASA, Coxibs

**What dose for colchicine in acute gout?**
- Colchicine has traditionally been dosed very high, leading to almost routine gastrointestinal (GI) disturbances 23
- 1 RCT investigated this traditional dosing: (N=43) in 1987 compared placebo vs colchicine 1mg po stat, followed by 0.5mg po q2h until attack stopped or they felt too ill to continue colchicine. 24
  - Max therapy: 12 tablet attack: o NNT to reduce clinical symptoms: pain, tenderness, redness, swelling = 2; NNT to reduce pain = 3
  - o NNN to cause diarrhea/vomiting = 1
- Uncontrolled reports show that colchicine 0.6mg BID-TID (or less) is effective while reducing GI side effects 2
- FDA recently updated dosing of colchicine in gout: 1.2 mg (2 tablets) at the first sign of the flare followed by 0.6 mg (1 tablet) one hour later. Max recommended dose for gout flares is 1.8 mg over a 1 hour period.
- Patients with reduced renal function may tolerate colchicine as long as well hydrated (0.6mg BID-TID x2d, daily x7d then discontinue or ↓ to every other day). (Avoid if possible if on dialysis. Avoid if history of solid organ transplant.)

**Allopurinol, etc. for Prophylaxis?**
- Allopurinol can be used in both over-producers & under-excreters. Using allopurinol to maintain a serum uric acid (SUA) level of 274-393μmol/L has shown a 30% risk reduction in recurrent gout attacks 25
  - It should not be started, stopped or changed in an acute attack as this can destabilize uric acid crystals.
  - Consider if ≥3 attacks/year, or Trisk (e.g. chemotherapy, ↑ SUA levels, advanced disease)
- Doses should be individualized and titrated (range: 50mg every other day to ≤800mg daily)
- CKD as a rule of thumb if CIcr ≤50ml/min, start at 50mg, with 50mg ↑1/day (MAX 300mg/d). {More complicated dosing regimens also available (see CPS)}
- Elderly: consider every other day initial dosing 26
  - Risks vs benefit becomes less clear as age increases.
- Prophylaxis with colchicine or an NSAID (for ~3-6+ months) is recommended when initiating allopurinol.
- Significant side effects include hypersensitivity and Stevens Johnson syndrome. (Also rash, diarrhea.)

**What is the role of steroids in gout?**
- Short-term corticosteroids may be an option for acute attacks when unable to use NSAIDS or colchicine [e.g. Depot-Medrol 40-80mg x1 IM, prednisone 25-50mg PO x 3-5 days or intra-articular (IA) injection x1] 1.
  - Short courses (≤ 2 wks) do not require tapering.
- A review of 3 trials (N=74) comparing corticosteroids to NSAIDs showed that corticosteroids to be equally effective, with fewer side effects if used short-term 29
  - If frequent or prolonged use, side effects can be minimized with local injections. Uncontrolled trial using tramadol intra-articularly (IA) showed pain relief within 48hrs in all 19 patients 30

**Miscellaneous**
- 1600kcal/day diet for 16 weeks ↓ SUA by 100μmol/L 31
- ASA: Low-dose (~2g/day) more greatly associated with gout attacks; >2g ASA is uricosuric; In 21 prevention, the CV benefits of low-dose ASA likely outweigh the risks of precipitating a gout attack.

**Extras**
- Losartan & fenofibrate have some uricosuric effects 23
- Fexofenadine (Ulorid®) used in Europe & recently FDA approved; a xanthine oxidase-inhibitor not chemically related to allopurinol; may be equivalent to allopurinol in preventing attacks (may be superior in decreasing uric acid levels); may be safer option in renal dysfunction; more study needed
- Uricase – a biotechnology drug still in testing stages; enzyme not produced by humans which helps to break down uric acid
- Oxypurinol, a metabolite of allopurinol is currently in clinical trials; theoretically less side effects
- Rilonacept (Arcalyst®) a potential competitor for colchicine

*Warm off the press!* Vitamin C shown to be independently associated with lower risk of gout. Published in Mar 9, 2009 edition of Archives of Internal Medicine 34. A 20 year observational study showed that vitamin C intake reduced risk of gout in men who took >250mg/day. The benefits were seen with ingestion of 500mg/day, furthermore, even greater reductions in risk were observed if 1000 or 1500mg/day. But caution: low urinary pH may increase kidney stone formation.
Case: Acute attack

A 46yo male presents to you, his family physician, having had excreting pain in his big toe last night. This is the 3rd occurrence in the last 3 months. Advil has worked the last 2 times to get rid of it, but the initial pain is so bad that it keeps him up all night. His dad, who had the same problems, suggested he cut down on the amount of beer he drinks, but he doesn’t think that it’s working and he wants something that’ll be effective!

You’ve known this patient for many years, he is obese and has slightly elevated LDL. On the bright side, the smoking cessation plan you created together was successful and he has been smoke-free for 2 years. Upon further examination of his toe you find it is warm, swollen, and he is very guarded.

Would you prescribe anything? If so, what?

Is this patient a candidate for preventative therapy? If so, which agent would you choose?

How would you initiate therapy? What would you monitor?

What would be the goal of therapy if the patient had a history of a solid organ transplant, heart failure and GI bleeds?

What if the patient were 75 years old with renal disease but otherwise healthy?

References – RxFiles Newsletter : Gout (2009)


2 Wortmann RL. Recent advances in the management of gout and hyperuricemia. Curr Opin Rheumatol. 2006; 18(2):144-149.


