Open Label Randomized Pragmatic Trial (CONTACT) Comparing Naproxen and Low-Dose Colchicine for the Treatment of Gout Flares in Primary Care

BACKGROUND:

- Gout affects approximately 3.8% of U.S. adults.
- NSAIDs effectively treat gout flares but have side effects.
- Colchicine at high doses is effective but also has side effects. Low-dose colchicine regimens have been proposed, but their efficacy and tolerability have not been evaluated.

OBJECTIVE:

- To compare the efficacy and safety of naproxen and low-dose colchicine for treating gout flares

METHODS:

- **Design**: Multicenter, open-label, randomized parallel trial
- **Duration**: 4 weeks
- **Inclusion criteria**: Patients 18 years and older presenting to a primary care practitioner with a current gout flare. Diagnosis of gout was made without joint aspiration, blood tests, or imaging.
- **Exclusion criteria**: Unstable medical conditions (ischemic heart disease, impaired liver function), stage 4/5 chronic kidney disease, recent surgery, recent gastrointestinal bleed, history of gastric ulcer, allergy to aspirin or NSAIDs, previous inability to tolerate naproxen or colchicine, contraindications to either study drug, pregnant or breastfeeding patients, patients taking anticoagulants or who used naproxen or colchicine within 24 hours
- 399 patients were enrolled (200 in the naproxen group and 199 in the colchicine group) and randomized to receive either:
  - Naproxen 750 mg (3 tablets) initially, then 250 mg (1 tablet) every 8 hours for up to 7 days. At the practitioner's discretion, proton-pump inhibitors may have been prescribed.
  - Colchicine 500 mcg (1 tablet) every 8 hours for 4 days.
- **Primary outcome measure**: Change in pain intensity from baseline measured over the first 7 days
- **Secondary outcome measures**: Time-to-treatment effect; complete pain resolution; self-reported side effects; patient global assessment of treatment response; use of corticosteroids, paracetamol, NSAIDs, or opiates for gout pain; quality of life; adherence; relapse/recurrent gout flare; absence from work/education; attendance at practitioner's office, emergency department, or primary care office. A cost utility analysis was also undertaken.
- 90% power was calculated for 200 patients in each group allowing for 20% loss to follow-up to detect a standardized effect size of 0.3
- Both intent-to-treat and per-protocol data handling methods were used.

RESULTS:

- **Primary outcome measure**:
  - Over days 1-7, both groups had within-group improvements with no significant differences in mean change in worst pain intensity between the two groups (colchicine vs. naproxen: adjusted mean difference -0.18; 95% CI -0.53 to 0.17; p=0.32)
- **Secondary outcome measures**:
  - More patients in the colchicine group used paracetamol or codeine than those in the naproxen group for gout during the first 7 days. Ibuprofen use was more common in the colchicine group at week 4.
  - Naproxen was slightly less costly than low-dose colchicine.
  - Diarrhea and headache were more common with colchicine than naproxen (45.9% vs. 20.0%; OR 3.31 (95% CI 2.01 to 5.44, p<0.001) and 20.5% vs. 10.7%; OR 1.92 (95% CI 1.03 to 3.55, p=0.039), respectively. Constipation was less common with colchicine than naproxen group (4.8% vs. 19.3%; OR 0.24 (95% CI 0.11 to 0.54, p<0.001)).
  - No between-group differences in complete pain resolution and patient global assessment of treatment response were seen at any time point.

    - No between-group differences in relapse/recurrent gout flares, consulting other healthcare centers, or time off work were reported at week 4.
- **Author's conclusion**: There was no difference in pain intensity between those treated with naproxen or low-dose colchicine for gout flare over 7 days. However, naproxen caused fewer side effects.

STRENGTHS:

- Pragmatic design
- Randomized

LIMITATIONS:

- The inclusion and exclusion criteria did not take existing comorbidities, use of urate-lowering therapy, or prior gout flare rates into consideration.
- Open-label design
- Use of drugs that could affect uric acid concentrations, e.g., thiazide diuretics, was not assessed
- Objective methods were not used to diagnose gout, which might have led to the inaccurate determination of an acute gout attack. The researchers could have performed joint fluid tests to assess for urate crystals, blood tests to measure uric acid levels, or imaging tests to detect presence of crystals or to rule out other non-gout joint problems
- Outcome measures were self-reported.
- Over 86% of patients in each group were males. Gout is more common in males but this study proportion is still higher than that of the general population.
- How the factors used for the cost-analysis determination compare to costs in the U.S. (e.g., doctor's visits, medications, etc.) is unclear.

CONCLUSION:

- Both naproxen and low dose colchicine produced pain relief from an acute gout flare, with no significant differences in pain reduction between therapies and similar patient ratings of complete pain relief and global treatment response. However, naproxen resulted in fewer side effects such as diarrhea and headache. Naproxen was also associated with a slightly lower cost and less use of additional medications for pain relief.
- Future research should compare low-dose colchicine or naproxen to other medications used to treat gout flares like corticosteroids.

Reference: Roddy E, Clarkson K, Blagojevic-Bucknall M, Mehta R, Oppong R, Avery A, et al. Open-Label Randomized Pragmatic Trial (CONTACT) Comparing Naproxen and Low-Dose Colchicine for the Treatment of Gout Flares in Primary Care. Ann Rheum Dis. 2020; 79(2): 276-284.

Corey A. Whetzel, PharmD Candidate
07.21.2020