TOOLS FOR PRACTICE #299 | October 4, 2021

TOOLS FOR PRACTICE

PEER PATIENTS EXPERIENCE EVIDENCE RESEARCH

Cardiovascular prevention trials: Now calling colchicine to the stand

CLINICAL QUESTION

Is colchicine effective for secondary cardiovascular prevention?

BOTTOM LINE

Daily low-dose colchicine in people with coronary artery disease (CAD) lowers the risk of cardiovascular events by ~1%/year (relative risk reduction 25-30%), but increases the risk of gastrointestinal events (mostly diarrhea) by ~2% and has no effect on mortality.

EVIDENCE

- At least 7 systematic reviews compared the effect of colchicine to placebo in addition to standard therapy in individuals with CAD [4-11 randomized controlled trials (RCTs), 5820-12869 participants, duration 5 days to 3 years].[1-7]
    - All showed similar:
        - Colchicine reduced cardiovascular events [relative risk reduction (RRR) ~30%].
        - No difference in mortality.
        - Most meta-analyses evaluating gastrointestinal events found ~2% absolute risk with colchicine (mostly diarrhea).[2,3,6]

- Two largest placebo-controlled, good quality RCTs, non-industry funded:
    - LoDoCo2 trial[8] compared colchicine 0.5mg daily versus placebo for 2.5 years in 5522 participants (age≈66, 15% female) with stable CAD.
        - Cardiovascular events (cardiovascular mortality, myocardial infarction, ischemic strokes, urgent revascularization): Colchicine 6.8% versus 9.6% placebo, RRR=29%, number needed to treat (NNT)=36.
        - No significant difference in mortality (2.6% versus 2.2%).
        - No difference in adverse events except myalgias (NNH=38).
    - COLCOT trial[9] compared colchicine 0.5mg daily versus placebo for 23 months in 4745 participants (age≈61, 19% female) within 1 month after myocardial infarction.
        - Cardiovascular events (cardiovascular mortality, myocardial infarction, strokes, urgent revascularization): Colchicine 5.5% versus 7.1% placebo, RRR=24%, NNT=63.
        - No difference in mortality (1.8% in both groups).
        - No difference in any or serious adverse events.
- Limitations: Excluded individuals with various risk factors for colchicine toxicity (examples kidney or muscular disease) and one trial[8] had an open-label colchicine run-in period that excluded 15% of patients before randomization, mostly because of adverse events.

CONTEXT

- Recent guidelines for secondary prevention in CAD or post-myocardial infarction do not make any recommendations about colchicine.[10,11]
- The new 0.5mg dose costs ~$45 for a 3-month supply (versus $25 for 0.6mg dose).[12,13]
- Colchicine efficacy on cardiovascular events better [example ezetimibe (RRR ~6%)] or comparable [example aspirin or statins (RRR~25%)] to other preventive therapies, but without the benefits on mortality of aspirin and statins.[14,15]

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AUTHORS

Nicolas Dugré, PharmD MSc BCACP, **Stéphane Vanier,** MD CCFP**, Ricky D Turgeon,** BSc (Pharm) ACPR PharmD

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