GEMs
GOOD EVIDENCE MATTERS

GEMs of the Week

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What's in this week's issue?

Week of September 13 - 17, 2021

SPOTLIGHT: Considering Decreased Aspirin Dose in Cardiovascular Disease

- Does Chiropractic Care Provide Added Benefits to Treating Low Back Pain for Young Military Personnel?
- Can the Sunshine Vitamin Help Prevent Severe Asthma Exacerbations in Children?

Considering Decreased Aspirin Dose in Cardiovascular Disease

GEMs GOOD EVIDENCE MATTERS SPOTLIGHT

Comparative Effectiveness of Aspirin Dosing in Cardiovascular Disease

Jones WS, Mulder H, Wruck LM, et al. Comparative Effectiveness of Aspirin Dosing in Cardiovascular Disease. *N Engl J Med*. 2021; 384(21):1981–1990. doi:10.1056/NEJMoa2102137

KEY TAKEAWAY: There are no significant differences between 81 mg and 325 mg of aspirin (ASA) when comparing the incidence of significant cardiovascular events or major bleeding in patients with atherosclerotic cardiovascular disease (ASCVD).

STUDY DESIGN: Randomized controlled trial

LEVEL OF EVIDENCE: STEP 2

BRIEF BACKGROUND INFORMATION: The leading cause of death in the US is atherosclerotic coronary artery disease (CAD) and patients with risk factors for cardiovascular events and with a history of cardiovascular events are commonly prescribed ASA to prevent future events. Current literature does not offer definitive guidance on proper dosing for the prevention of cardiovascular events or adverse events such as major bleeding.

PATIENTS: US adults with ASCVD

INTERVENTION: 81 mg ASA

CONTROL: 325 mg ASA

OUTCOME:

Efficacy Outcomes – Composite of deaths from any cause, hospitalizations for MI, hospitalizations for CVA

Safety Outcomes – Hospitalizations for major bleeding

METHODS (BRIEF DESCRIPTION):

- Inclusion Criteria: Adults with pre-existing ASCVD (prior MI, prior angiography showing ≥75% stenosis of at least one epicardial coronary vessel, prior PCI, or prior CABG)
- Within 5 years before enrollment:
  - 35.3% had prior MI.
  - 53% had previous coronary revascularization procedures.
  - 96% had been taking ASA daily.
    - 85.3% took 81 mg
    - 2.3% took 162 mg
    - 12.2% took 325 mg
  - 22.3% were taking P2Y12 inhibitors.
- Exclusion Criteria: Patients using oral anticoagulants or ticagrelor at the time of randomization or during the study period.
- Location: USA
- Type of Study: Open-label, non-blinded study in which 15,065 patients were randomly assigned to 81 mg and 325 mg groups followed every 3 or 6 months.

INTERVENTION (# IN THE GROUP): 7,540

COMPARISON (# IN THE GROUP): 7,536

FOLLOW UP PERIOD: Average of 26.2 months

RESULTS: There were no differences between groups taking 81 mg and 325 mg ASA in all outcomes.

- Death from any cause (Hazard Ratio [HR] 0.87; 95% CI, 0.75–1.0)
- Hospitalization for MI (HR 1.1; 95% CI, 0.88–1.3)
- Hospitalization for stroke (HR 1.1; 95% CI, 0.82–1.5)
- Occurrence of CABG or PCI (HR 1.0; 95% CI, 0.92–1.2)
- Hospitalization for TIA (HR 0.79; 95% CI, 0.44–1.4)
- Hospitalization for major bleeding associated with blood product transfusion (HR 1.2; 95% CI, 0.79–1.8)

LIMITATIONS: There were some participants that left the study and others that switched from 325 mg to 81 mg mid-study.

Mitesh Patel, MD
HCA LewisGale Medical Center FMRP
Roanoke, VA

Does Chiropractic Care Provide Added Benefits to Treating Low Back Pain for Young Military Personnel?

Effect of Usual Medical Care Plus Chiropractic Care vs Usual Medical Care Alone on Pain and Disability Among US Service Members with Low Back Pain

Goertz CM, Long CR, Vining RD, Pohlman KA, Walter J, Coulter I. Effect of Usual Medical Care Plus Chiropractic Care vs Usual Medical Care Alone on Pain and Disability Among US Service Members With Low Back Pain: A Comparative Effectiveness Clinical Trial. *JAMA Netw Open*. 2018; 1(1):e180105. Published 2018 May 18. doi:10.1001/jamanetworkopen.2018.0105

KEY TAKEAWAY: The use of chiropractic care can provide moderate short-term benefits in the management of lower back pain (LBP) when used in addition to usual medical care (UMC) in active-duty military personnel.
STUDY DESIGN: Prospective, multisite, parallel-group comparative effectiveness clinical trial
LEVEL OF EVIDENCE: STEP 3

BRIEF BACKGROUND INFORMATION: Lower back pain is the second leading cause of disability with direct costs estimated at $34 billion in 2010. Chiropractic care has been used in the past but tangible evidence showing applicability in younger populations has been lacking.

PATIENTS: Active-duty US military personnel 18 to 50 years old reporting LBP
INTERVENTION: Usual medical care + up to 12 chiropractic visits (spinal manipulative therapy)
CONTROL: Usual medical care
OUTCOME: Average lower back pain intensity and functional disability

METHODS (BRIEF DESCRIPTION):

- Active-duty US military personnel from 2 large military medical centers in major metropolitan areas 18 to 50 years old reporting LBP were allocated to either:
  - UMC: Self-management advice, pharmacologic pain management, physical therapy, or pain clinic; or
  - UMC with chiropractic care.
- Primary outcomes were measured at baseline and 2, 4, 5, and 12 weeks via online self-report questions.
- Outcomes included:
  - Average lower back pain intensity measured using a rating scale from 0 (no LBP) to 10 (worst possible LBP); and
  - Functional disability related to lower back pain assessed by the Roland Morris Disability Questionnaire (0–24, higher scores indicate more disability).

INTERVENTION (# IN THE GROUP): 375
COMPARISON (# IN THE GROUP): 375

FOLLOW UP PERIOD: 12 weeks

RESULTS: UMC + chiropractic care improved outcomes more than UMC alone.

- LBP intensity (mean difference [MD] –1.1; 95% CI, –1.4 to –0.7)
- Disability (MD –2.2; 95% CI, –3.1 to –1.2)
- Similar findings with significance at week 12, but with lesser magnitude.

LIMITATIONS:

- Due to the nonspecific nature of LBP, patient heterogeneity exists which is difficult to account for in the analysis.
- Patients in the treatment group received more multimodal care and indirectly longer patient care.
- Treatment modalities that are applied in both groups makes it difficult to analyze which components of both UMC and chiropractic interventions were associated with beneficial effects.
- Relatively short follow up of 12 weeks.

Selamawi Mesfin, MD & William Gallagher, MD
The MedStar Health/Georgetown – Washington Hospital Center FMRP
Washington D.C.

Can the Sunshine Vitamin Help Prevent Severe Asthma Exacerbations in Children?

Effect of Vitamin D_3 Supplementation on Severe Asthma Exacerbations in Children with Asthma and Low Vitamin D Levels: The VDKA Randomized Clinical Trial

Forno E, Bacharier LB, Phipatanakul W, et al. Effect of Vitamin D_3 Supplementation on Severe Asthma Exacerbations in Children With Asthma and Low Vitamin D Levels: The VDKA Randomized Clinical Trial [published correction appears in *JAMA*. 2021 Jul 6;326(1):90]. *JAMA*. 2020; 324(8):752–760. doi:10.1001/jama.2020.12384

KEY TAKEAWAY: Taking vitamin D supplements does not reduce the time for asthmatic children with low vitamin D levels to have a severe exacerbation.

STUDY DESIGN: Double-blind, randomized placebo-controlled clinical trial

LEVEL OF EVIDENCE: STEP 2

BRIEF BACKGROUND INFORMATION: Asthma is one of the most common chronic conditions, significantly affecting the daily activities of children and their quality of life. Some past studies have shown that low vitamin D levels may be associated with severe asthma exacerbations and an inferior response to corticosteroids. However, no studies have demonstrated if vitamin D supplementation would help reduce the time to a severe exacerbation in children.

PATIENTS: Children 6 to 16 years old with persistent asthma and low vitamin D levels

INTERVENTION: Daily vitamin D_3 4,000 IU

CONTROL: Daily placebo capsules

OUTCOME: Time to next severe asthma exacerbation

Secondary Outcomes: Time to a viral-induced exacerbation, 50% reduction in dose of inhaled steroids at the midway point of the study, and 50% reduction in cumulative inhaled steroid dose throughout the study

METHODS (BRIEF DESCRIPTION):

- Patient Population: 6–16 year olds with asthma and vitamin D levels <30 ng/ml and >10 ng/ml from 7 clinic sites across the US.
- Inclusion Criteria: Children diagnosed with asthma for at least 1 year, 1 severe asthma attack within the year prior, has used asthma medications for at least 6 months in the year prior, FEV1 ≥ 70% of predicted, and bronchodilator responsiveness or increased airway responsiveness.
- Exclusion Criteria: Other chronic respiratory diseases, chronic oral corticosteroid treatment, severe asthma, and the inability to do a spirometry test successfully.
- Randomization occurred after a 4-week run-in period where all participants took only placebo capsules (same look to the vitamin D_3 capsules) and inhaled fluticasone (88 µg twice a day for ages 6–11 years and 100 µg twice a day for ages ≥12) and albuterol as needed.
- Treatment Arm: At randomization, the intervention group switched placebo capsules to 4,000 IU vitamin D_3 daily. All participants in both groups continued the inhaled fluticasone and were followed for 48 weeks.
- Vitamin D levels were monitored at time of randomization and then at 16, 32, and 48 weeks.
- Participants had 6 in-person visits every 2 months with phone visits in between.
- At 24 weeks, all participants whose asthma was well controlled based on the Asthma Control Test (ACT) with a score of 19, had their fluticasone dose decreased by 50%.

INTERVENTION (# IN THE GROUP): 96

COMPARISON (# IN THE GROUP): 96

FOLLOW UP PERIOD: 48 weeks

RESULTS:

Primary Outcome:

- Vitamin D supplementation did not improve the time it took asthmatic children to have a severe exacerbation compared to placebo (240 vs 253 days respectively; mean group difference –13.1; 95% CI, –42.6 to 16.4) (adjusted HR 1.1; 95% CI, 0.69–1.9).

Secondary Outcomes:

- Vitamin D supplementation did not reduce the time it took for a severe asthma exacerbation to occur due to a viral etiology vs the placebo group (mean group difference –9.1 days; 95% CI, –36 to 17) (adjusted HR 1.3; 95% CI, 0.63–2.8).
- There was not a significant difference between the number of children who could reduce their

fluticasone dose by 50% at 24 weeks in the vitamin D supplement group vs placebo (31% vs 32% respectively; mean group difference –1.1%; 95% CI, –15 to 12).

- There was no significant decrease in the cumulative fluticasone dosage during the study between the vitamin D group vs placebo (60 mg vs 55 mg; mean group difference 4.4 mg; 95% CI, –0.99 to 9.8).

LIMITATIONS:

- Vitamin D and placebo groups both had lower than anticipated rates of severe asthma attacks. Since the study was not adequately powered, it was difficult to determine if the differences were statistically significant.
- The findings cannot be applied to other age groups or populations where monitoring vitamin D levels would be limited.

Vinusiya Shanmugalingam, MD
Indiana University School of Medicine Arnett FMR
Lafayette, IN