GEMs
GOOD EVIDENCE MATTERS

GEMs of the Week

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What's in this week's issue?

Week of January 9 - 13, 2023

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- Very High HDL-C in CAD: Too Much of a "Good" Thing?
- Improving IUD IQ with Simulation and Video Training

Does Pacifier Use Worsen Breastfeeding Outcomes?

GEMs GOOD EVIDENCE MATTERS SPOTLIGHT

Pacifier Use and Breastfeeding in Term and Preterm Newborns: A Systematic Review and Meta-Analysis

Tolppola O, Renko M, Sankilampi U, Kiviranta P, Hintikka L, Kuitunen I. Pacifier use and breastfeeding in term and preterm newborns-a systematic review and meta-analysis. *Eur J Pediatr*. 2022;181(9):3421-3428. doi:10.1007/s00431-022-04559-9

KEY TAKEAWAY: Pacifier use is not associated with worse breastfeeding outcomes and should not be restricted in newborns.

STUDY DESIGN: Systematic review and meta-analysis of 10 RCTs, with five analyzing preterm infants (N=602) and five analyzing term infants (N=2,843)

LEVEL OF EVIDENCE: STEP 1

BRIEF BACKGROUND INFORMATION: The World Health Organization currently recommends counseling mothers on the risk of pacifier use on breastfeeding. While pacifier use has been associated with some negative breastfeeding outcomes in observational studies, these outcomes have not been found in RCTs. Further evaluation is needed on the effects of pacifier use on breastfeeding outcomes.

PATIENTS: Newborns up to six months old

INTERVENTION: No use or restriction of pacifiers

CONTROL: Use or no restriction of pacifiers

PRIMARY OUTCOME: Breastfeeding rates

Secondary Outcomes: Hospital stay duration, time to achieve full oral feeding in preterm newborns

METHODS (BRIEF DESCRIPTION):

- Four databases were used to identify 10 multi-national RCTs evaluating the effects of free and restricted pacifier use in newborns.
- Risk of bias assessed via the Cochrane Risk of Bias Tool 2.0.
- Breastfeeding rates were analyzed at two, three, four, and six months.
- Term infants: Intervention group restricted pacifier during hospital stay and up to age three months.
- Preterm infants: Intervention group provided pacifier for use during hospital stay.

INTERVENTION (# IN THE GROUP): 1,710

- Term: 1,427
- Preterm: 283

COMPARISON (# IN THE GROUP): 1,705

- Term: 1,416
- Preterm: 289

FOLLOW UP PERIOD: Six months

RESULTS:

Primary Outcome –

- Pacifier use was not associated with lower breastfeeding rates compared to restriction of pacifier use in term newborns.
  - Two months: RR 1.0 (95% CI, 0.98–1.03)
  - Three months: RR 1.0 (95% CI, 0.98–1.03)
  - Four months: RR 1.0 (95% CI, 0.99–1.1)
  - Six months: RR 1.0 (95% CI, 0.92–1.2)
- Pacifier use was not associated with lower breastfeeding rates compared to no pacifier use in preterm newborns.
  - Three months: RR 1.1 (95% CI, 0.81–1.5)
  - Six months: RR 1.3 (95% CI, 0.86–1.8)

Secondary Outcomes –

- Preterm newborns with pacifier use in the hospital had a shorter duration of hospital stay compared to no pacifier use (MD 7.2 days; 95% CI, 4.0–10).
- Pacifier use resulted in shorter transition time from gavage to full oral feeding compared to no pacifier use in preterm infants (MD 3.2 days; 95% CI, 1.1–5.2).

LIMITATIONS:

- Studies that evaluated preterm neonates had small sample sizes.
- Several studies included did not describe the randomization process in entirety.
- Blinding in several studies was limited.
- Potential bias was high in several of the studies included.
- Several studies deviated from the intended intervention.
- Outcome measurements varied in several studies.

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COPD and Corticosteroids: Does Dosing Matter in Exacerbations?

Personalized Variable vs Fixed Dose Systemic Corticosteroid Therapy in Hospitalized Patients with Acute Exacerbations of COPD

Li L, Zhao N, Ma X, et al. Personalized Variable vs Fixed-Dose Systemic Corticosteroid Therapy in Hospitalized Patients with Acute Exacerbations of COPD: A Prospective, Multicenter, Randomized, Open-Label Clinical Trial. *Chest*. 2021;160(5):1660-1669. doi:10.1016/j.chest.2021.05.024

KEY TAKEAWAY: Personalized dosing of corticosteroids in patients with chronic obstructive pulmonary disease (COPD) with exacerbation reduces the risk of in-hospital treatment failure but does not significantly impact post-discharge outcomes, hospital length of stay, or cost.

STUDY DESIGN: Prospective, randomized, unblinded, multi-site, open label study

LEVEL OF EVIDENCE: STEP 2

BRIEF BACKGROUND INFORMATION: Corticosteroids are a staple of COPD exacerbation treatment. While corticosteroids clearly improve patient outcomes, prior studies have varied on ideal corticosteroid dosing.

PATIENTS: Hospitalized adults with COPD exacerbation

INTERVENTION: Personalized dosing of prednisolone

CONTROL: Fixed dosing of prednisolone

PRIMARY OUTCOME: Combination of in-hospital treatment failure and medium-term failure

METHODS (BRIEF DESCRIPTION):

- Investigators included adults ≥40 years old presenting with acute COPD exacerbation to multiple hospitals in China.
- Exclusion criteria included asthma, steroid use within one month, imaging suggesting pneumonia, pneumothorax, or pulmonary embolism, left heart failure, uncontrolled hypertension, or the need for mechanical ventilation on admission.
- Patients were well balanced between the groups, including FEV1 and GOLD grade.
- More than 80% of the participants in each group were male, around 90% smoked, and around 10% were pre-treated with steroids.
- Patients were assigned in a 1:1 ratio to either the fixed-group or the personalized-dose group.
    - Investigators gave the personalized-dose group a calculated dose for five days which was based on body weight, Anthonisen type, COPD assessment score, previous corticosteroid use for COPD exacerbations, C-reactive protein (CRP), eosinophilia, and blood gas analysis.
    - Investigators gave the fixed-dose group 40 mg of prednisolone for five days.
- The primary outcome was a composite measure of treatment failure that included in-hospital treatment failure and post-discharge failure.
    - In-hospital failure was defined as need for invasive or noninvasive mechanical ventilation, additional treatment with corticosteroids or aminophylline, or upgrading co-administration of antibiotics due to persistent dyspnea, bronchospasm, or other respiratory symptoms.
    - Post-discharge failure defined as death or readmission because of COPD exacerbation within 180 days of discharge.
- Secondary outcomes included length of stay and cost.

INTERVENTION (# IN THE GROUP): 124

COMPARISON (# IN THE GROUP): 124

FOLLOW UP PERIOD: 180 days post-hospital discharge

RESULTS:

Primary Outcome –

- Personalized prednisolone dosing reduced the risk of the combined outcome of in-hospital and post-discharge failure as compared to the fixed-dose group (relative risk [RR] 0.4; 95% CI, 0.24–0.68).

Secondary Outcomes –

- Failure of therapy during the in-hospital stay was 11% in the personalized-dose group versus 24% in the fixed-dose group (RR 0.37; 95% CI, 0.18–0.74).
- Failure of therapy during the medium-term follow-up period of 180 days was not significantly different.
- Hospital length of stay and costs were similar for the two groups.

LIMITATIONS:

- Patient population was ecologically biased and may not reflect the baseline characteristics of other populations (BMI, body weight).
- The five-factor dosing scale utilized to calculate prednisolone dose for the personalized-dose group has not been validated outside of this study.
- The study was open-label and may have been open to biases in assessing treatment failure.

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Very High HDL-C in CAD: Too Much of a "Good" Thing?

Association Between High-Density Lipoprotein Cholesterol Levels and Adverse Cardiovascular Outcomes in High-Risk Populations

Liu C, Dhindsa D, Almuwaqqat Z, et al. Association between high-density lipoprotein cholesterol levels and adverse cardiovascular outcomes in high-risk populations. *JAMA Cardiol*. 2022 Jul 1;7(7):672-680.

KEY TAKEAWAY: Very high levels of HDL-C significantly increase all-cause mortality in patients with known CAD.
STUDY DESIGN: Prospective cohort study
LEVEL OF EVIDENCE: STEP 3

BRIEF BACKGROUND INFORMATION: Elevated levels of high-density lipoprotein cholesterol (HDL-C) have long been thought to be associated with lower risk for cardiovascular disease (CVD). However, recent evidence shows that high HDL-C is associated with higher mortality among patients without CVD. It is unknown if there is an association between very high HDL-C and mortality risk in patients with coronary artery disease (CAD).

PATIENTS: Adults with CAD
INTERVENTION: Elevated HDL-C levels
CONTROL: Normal HDL-C levels
PRIMARY OUTCOME: All-cause mortality
Secondary Outcome: Cardiovascular mortality

METHODS (BRIEF DESCRIPTION):

- A prospective multicenter cohort study included patients with confirmed CAD from the United Kingdom Biobank (UKB: 2006–2020) and the Emory Cardiovascular Biobank (EmCAB: 2003–2020) in Atlanta, Georgia.
  - UKB (N=14,478): mean 62 years old, 76% men, 93% White
  - EmCAB (N=5,467): mean 63 years old, 66% men, 73% White
- Levels of HDL-C were compared:
  - Very Low: <30 mg/dL
  - Low: 30–40 mg/dL
  - Normal: 40–60 mg/dL
  - High: 60–80 mg/dL
  - Very High: >80 mg/dL

INTERVENTION (# IN THE GROUP): 345
COMPARISON (# IN THE GROUP): 10,027

FOLLOW UP PERIOD: 6.7–8.9 years

RESULTS:
Primary Outcome –

- Elevated HDL-C levels significantly increased all-cause mortality compared to normal HDL-C levels among patients with CAD in both UKB and EmCAB groups.
  - UKB (hazard ratio [HR] 2.0; 95% CI, 1.4–2.7)
  - EmCAB (HR 1.6; 95% CI, 1.1–2.3)

Secondary Outcome –

- Elevated HDL-C levels significantly increased CVD-related mortality compared to normal HDL-C in the UKB group but not the EmCAB group.
  - UKB (HR 1.7; 95% CI, 1.1–2.7)
  - EmCAB (HR 1.6; 95% CI, 0.9–2.6)

LIMITATIONS:

- The size of the two groups were different, with the UKB group being significantly larger.
- The two groups utilized different CAD selection criteria.
  - UKB: ICD-10
  - EmCAB: left heart catheterization

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Improving IUD IQ with Simulation and Video Training

Using Video Modules and Simulation Learning to Improve IUD Counseling Among Internal Medicine Residents – A Randomized Controlled Educational Trial

Hirsch H, Batur P, Spencer AL, McNamara M. Using Video Modules and Simulation Learning to Improve IUD Counseling Among Internal Medicine Residents-a Randomized Controlled Educational Trial. *J Gen Intern Med*. 2021;36(5):1446-1447. doi:10.1007/s11606-020-05832-z

KEY TAKEAWAY: Multi-modal didactics may not improve residents' confidence performing IUD insertions compared to a traditional one-hour lecture.

STUDY DESIGN: Randomized control trial

LEVEL OF EVIDENCE: STEP 3 (downgraded due to small sample size)

BRIEF BACKGROUND INFORMATION: Teaching faculty have identified a lack of knowledge and confidence about IUD procedures and counseling among residents. This study sought to determine if video modules and hands-on IUD simulation workshops in addition to traditional resident lectures would improve comfort and ability to counsel about IUDs.

PATIENTS: Internal medicine residents

INTERVENTION: Multi-modal didactics on IUD counseling and placement

CONTROL: Traditional one-hour lecture

PRIMARY OUTCOME: Confidence and ability to counsel and perform IUD insertions

Secondary Outcomes: Knowledge about IUDs, number of referrals for IUDs

METHODS (BRIEF DESCRIPTION):

- 58 Internal Medicine Residents at Brigham and Women's Hospital were randomized into intervention group or control group.
- The intervention group received multi-modal curriculum didactics on IUD counseling and placement. This included a one-hour video module, a seven-minute video showing a mock patient encounter, as well as a hands-on simulation workshop on plastic models.
- The comparison group received the traditional one-hour lecture training on contraceptive care.
- Primary and secondary outcomes were measured with pre- and post-curriculum surveys.
  - Resident knowledge was assessed using a 13-question survey.
  - Resident confidence was assessed using a five-question, on a five-point Likert scale.
  - Residents reported, per their recollection, the number of referrals placed for IUD placement.

INTERVENTION (# IN THE GROUP): 34

COMPARISON (# IN THE GROUP): 24

FOLLOW UP PERIOD: 2.5 years

RESULTS:

Primary Outcome –

- There was no significant increase in comfort and ability to counsel on IUDs after multi-modal didactics compared to traditional one-hour lecture (47% vs 27%, respectively; *P*=.054).

Secondary Outcomes –

- There was no significant difference in knowledge on IUDs after multi-modal didactics compared to traditional one-hour lecture (9.3 vs 9.0, respectively; *P*=.53).
- There was no significant difference in IUD referrals after multi-modal didactics compared to traditional one-hour lecture (24% vs 8.6%, respectively; *P*=.24).

LIMITATIONS:

- The study's sample size was not large enough to determine differences between the two groups. Thus, the impact of the multimodal curriculum could be elucidated further if studied on a larger scale.
- Recall bias may have impacted the number of referrals reported for IUD placement.
- The study did not discuss barriers to IUD counseling and referrals among residents. Multi-modal teaching could be improved through expanding to include open-ended discussions among residents on contraception counseling and barriers in healthcare.

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