GEMs
GOOD EVIDENCE MATTERS

GEMs of the Week

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What's in this week's issue?

Week of May 24 - 28, 2021

SPOTLIGHT: Hypertension - How low can you go?

- Further Evidence to Make a Change in Practice for Systolic Heart Failure
- Reflective Material Can Decrease Time Under Bili Lights

Hypertension: How low can you go?

GEMs GOOD EVIDENCE MATTERS SPOTLIGHT

Blood pressure targets in adults with hypertension

Arguedas JA, Veiva V, Wright JM. Blood pressure targets in adults with hypertension. *Cochrane Database Syst Rev.* 2020; 12:CD004349. Published 2020 Dec 17. Doi:10.1002/14651858.CD004349.pub3

KEY TAKEAWAY: The benefits of a lower blood pressure target of 135/85 rather than the standard blood pressure target of 140/90 do not outweigh the harms.
STUDY DESIGN: Systematic review and meta-analysis of 11 randomized controlled trials
LEVEL OF EVIDENCE: STEP 1

BRIEF BACKGROUND INFORMATION: In the past, the strategy of "the lower the better" was prevalent among physicians treating hypertension for the ideal blood pressure goal. However, this method was abandoned in the past decade due to a lack of supporting evidence, and physicians have agreed to use 140/90 mmHg as the standard blood pressure target. Recently, trials have reviewed the suggestion of a lower blood pressure target. This study attempts to investigate the latest trials and resolve the ongoing debate of whether a lower blood pressure target will lead to improved mortality and morbidity.

PATIENTS: Adults with hypertension
INTERVENTION: Target blood pressure of ≤135/85
CONTROL: "Standard therapy" (target blood pressure of ≤140/90)
OUTCOME: Mortality and serious adverse events

METHODS (BRIEF DESCRIPTION):

- Only adults (>18 years) that had at least two elevated blood pressures documented or were currently undergoing treatment for hypertension were included.
- Other inclusion criteria varied among the 11 randomized controlled trials (38,688 participants):
  - A specific baseline systolic blood pressure (SBP) was required for inclusion in 4 studies, and a specific baseline diastolic blood pressure (DBP) was required for inclusion in 4 studies. No restrictions in baseline pressures in 3 studies.
  - 2 studies only included diabetics, while 2 studies excluded diabetics
  - Nephropathy was an inclusion criterion in 3 studies
  - One study included only previous recent lacunar stroke
  - One study included only atrial fibrillation
- Trials compared participants of "lower" target blood pressure ≤135/85 vs participants of "standard" target blood pressure ≤140/90
- This study measured outcomes in total mortality and serious adverse events (myocardial infarction, stroke, congestive heart failure, end stage renal disease, etc.)
- The authors used risk ratio and a fixed-effect model to incorporate results from all trials.

INTERVENTION (# IN THE GROUP): 22,472
COMPARISON (# IN THE GROUP): 16,216

FOLLOW UP PERIOD: 1 to 7 years (weighted mean 3.7 years)

RESULTS:

- A lower blood pressure target compared to the standard of ≤140/90 does not decrease overall total mortality (11 trials, N=38,688; RR 0.95; 95% CI, 0.86–1.1) or serious adverse events (6 trials, N=18,165; RR 1.0; 95% CI, 0.99–1.1)
- Lower than standard blood pressure target may decrease the risk for myocardial infarction (6 trials, N=18,938; Absolute Risk Reduction [ARR] 0.4%; RR 0.84; 95% CI, 0.73–0.96; number needed to treat to benefit [NNTB] 250 over 3.7 years)
- Lower than standard blood pressure target may decrease the risk for congestive heart failure (5 trials, N=15,859; ARR 0.6%; RR 0.75; 95% CI, 0.60–0.92; NNTB 167 over 3.7 years)
- Lower than standard blood pressure target may increase the risk for other serious adverse events (6 trials, N=18,938; Absolute Risk Increase 3%; RR 1.4; 95% CI, 1.3–1.6; number needed to treat to harm [NNTH] 33 over 4 years)
  - These include hypotension, syncope, bradycardia or arrhythmia, hyperkalemia, angioedema, and renal failure

LIMITATIONS:

- Not generalizable to other populations because participants were primarily older adults with moderate to severe cardiovascular risk.
- Blood pressure goal was not blinded because of medication titration needed to achieve the blood pressure goal, and hence, high risk of performance and detection bias.
- Some patients weren't able to achieve the targeted blood pressure so were excluded from the study.

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Further Evidence to Make a Change in Practice for Systolic Heart Failure

Effects of Sacubitril/Valsartan on Physical and Social Activity Limitations in Patients with Heart Failure

Chandra A, Lewis EF, Claggett BL, et al. Effects of Sacubitril/Valsartan on Physical and Social Activity Limitations in Patients with Heart Failure: A Secondary Analysis of the PARADIGM-HF Trial. *JAMA Cardiology*, 2018; 3(6):498–505.

KEY TAKEAWAY: Sacubitril/Valsartan significantly improves overall physical and social activities in patients with heart failure with reduced ejection fraction when compared to enalapril.

STUDY DESIGN: Multicenter, randomized, double-blind, active treatment controlled clinical trial

LEVEL OF EVIDENCE: STEP 2

BRIEF BACKGROUND INFORMATION: Heart failure is a debilitating disease that results in multiple hospitalizations, poor quality of life, and increased mortality when management is not optimized. When compared to other chronic diseases, health related quality of life is significantly reduced in patients with heart failure, despite the standard of care.

PATIENTS: Patients ≥18 years old with heart failure

INTERVENTION: Oral Sacubitril/Valsartan 200 mg twice daily

CONTROL: Oral Enalapril 10 mg twice daily

OUTCOME: Physical and social limitations of health-related quality of life

METHODS (BRIEF DESCRIPTION):

- Inclusion Criteria: LVEF ≤40%, NYHA class II–IV, BNP >150 pg/ml, an NT-pro BNP >600 pg/ml, or heart failure associated hospitalization within 12 months of enrollment.
- All participants received enalapril 10 mg twice daily for 2 weeks and then 200 mg sacubitril/valsartan twice daily for 4 to 6 weeks.
- Participants were then randomized to twice daily enalapril 10 mg or twice daily sacubitril/valsartan 200 mg for 36 months to assess tolerance to treatment.
- Kansas City Cardiomyopathy Questionnaire (KCCQ) was used to assess physical and social limitations at baseline and at 4, 8, 12, 24 and 36 months.
- Predefined efficacy period: 8 months
- A multivariable linear regression analysis and sensitivity analysis were completed to account for missing data.

INTERVENTION (# IN THE GROUP): 4,187

COMPARISON (# IN THE GROUP): 4,212

FOLLOW UP PERIOD: 36 months

RESULTS:

Primary Outcome: Participants taking sacubitril/valsartan experienced greater improvements in physical and social activity at 8 months compared to the enalapril group (OR 1.1; 95% CI, 1.0–1.2)

Secondary Outcomes: Participants taking sacubitril/valsartan experienced significant improvements in the various components of physical and social activity at 8 months compared to the enalapril group.

- Sexual relationships (OR 1.2; 95% CI, 1.1–1.3)
- Household chores (OR 1.2; 95% CI, 1.1–1.3)
- Yardwork (OR 1.2; 95% CI, 1.1–1.3)
- Hobbies (OR 1.2; 95% CI, 1.1–1.3)
- Walking (OR 1.1; 95% CI, 1.0–1.2)

LIMITATIONS:

- Missing data of patients who died before the 8 month follow-up visit.
- Survivor bias in enalapril group due to increased rate of death.

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Reflective material can decrease time under bili lights

Use of reflective materials during phototherapy for newborn infants with unconjugated hyperbilirubinemia

Van Rostenbergh H, Ho JJ, Lim CH, Hamid IJA. Use of reflective materials during phototherapy for newborn infants with unconjugated hyperbilirubinemia. *Cochrane Database of Systematic Reviews*. 2020, Issue 7. Art No.: CD012011. DOI: 10.1002/14651851.CD012011.pub2

KEY TAKEAWAY: In infants with unconjugated hyperbilirubinemia the use of reflective materials during phototherapy is more effective at decreasing serum bilirubin levels, duration of phototherapy, and duration of hospital stay. However, the use of reflective materials has similar outcomes as double light therapy.
STUDY DESIGN: Systematic review of 12 RCTs
LEVEL OF EVIDENCE: STEP 1

BRIEF BACKGROUND INFORMATION: Neonatal hyperbilirubinemia is often treated with phototherapy. Increasing the light intensity can decrease the amount of time newborns need to be under lights. One way of increasing light intensity is by using reflective curtains around the bassinet.

PATIENTS: Infants with hyperbilirubinemia
INTERVENTION: Using reflective curtains around the light unit
CONTROL: Regular phototherapy without light intensity
OUTCOME: Bilirubin levels
Secondary: Duration of hospital stay & duration of phototherapy

METHODS (BRIEF DESCRIPTION):

- Term and preterm infants with unconjugated hyperbilirubinemia were chosen to participate.
- 11 studies used reflective materials (curtains of white plastic, linen, or aluminum) around the bilirubin unit compared to regular phototherapy without reflective material.
- One study compared reflective material used around the bilirubin unit to a double phototherapy unit.

INTERVENTION (# IN THE GROUP): 580
COMPARISON (# IN THE GROUP): No reflective materials = 495; Double phototherapy = 78

FOLLOW UP PERIOD: 4, 8, and 24 hours

RESULTS:
Primary Outcome: The use of reflective materials during phototherapy, compared to no reflective materials, decreased serum bilirubin levels at 4 to 8 hours (3 trials, N=281; Mean Difference [MD] –15µmol/L; 95% CI, –19 to –9.4; I^2=97%).

- The use of reflective materials during phototherapy did not decrease serum bilirubin levels consistently each hour.

Secondary Outcomes

- The use of reflective curtains during phototherapy significantly decreased the duration of hospital stay (2 trials, N=179; MD –41 hours; 95% CI, –46 to –36).
- 4 studies (N=231) indicated reflective curtains may decrease phototherapy duration when compared to the standard of care. However, a meta-analysis was not completed due to high heterogeneity (I^2=88%).

The use of reflective materials compared to double light therapy did not result in a significant difference in the decline of serum bilirubin levels (1 trial, N=156; MD 0.17; 95% CI, –8.6 to 8.9) or length of treatment time (1 trials, N=156; MD 4.0 hours; 95% CI, –1.6 to 9.6).

LIMITATIONS:

- Neonates with hemolysis were excluded.
- Different ages of infants may have affected outcomes.
- Only three studies supplied evidence of serum bilirubin levels at four to eight hours.

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