GEMs of the Week

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Simulation Training for Postpartum Hemorrhage

Does simulation improve clinical performance in management of postpartum hemorrhage?

Dillon SJ, Kleinmann W, Fomina Y, et al. Does simulation improve clinical performance in management of postpartum hemorrhage?. *Am J Obstet Gynecol.* 2021; 225(4):435.e1–435.e8. doi:10.1016/j.ajog.2021.05.025

KEY TAKEAWAY: Simulation training for response to postpartum hemorrhage improves time to administration of uterotonic medications, time to transfusion of blood products, and lower blood loss for women who experienced postpartum hemorrhage.

STUDY DESIGN: Prospective observational study

LEVEL OF EVIDENCE: STEP 2

BRIEF BACKGROUND INFORMATION: Postpartum hemorrhage continues to be one of the leading causes of severe morbidity and mortality for women in the United States and worldwide. Often postpartum hemorrhage is something that can be prevented if identified and treated in a timely manner. Two of the most common problems identified were delayed diagnosis as well as delayed time to treatment. Also, postpartum hemorrhage was found to be one of the top three leading preventable causes of death in Texas from 2012-2015. 50% of these deaths were deemed somewhat or very likely to have been preventable. This study aimed to examine the clinical performance and outcomes associated with postpartum hemorrhage because of uterine atony following the implementation of a multidisciplinary simulation program.

PATIENTS: Females with postpartum hemorrhage

INTERVENTION: Multidisciplinary simulation training

CONTROL: Pre-simulation training

OUTCOME: Timing to uterotonic medications and blood product administration

Secondary Outcome: Estimated blood loss

METHODS (BRIEF DESCRIPTION):

- This study was performed at Parkland Health and Hospital System, a large training hospital in Dallas, Texas.
- Patients who experienced postpartum hemorrhage as defined by ACOG (American College of Obstetrics and Gynecology) secondary to uterine atony requiring uterotonic medications and blood transfusion were included.
- The training included both nursing staff and resident physicians in obstetrics and anesthesia.
- Each simulation consisted of 15 minutes of simulated postpartum hemorrhage with 45 minutes of debriefing to follow.
- Epoch 1 took place before implementation of the simulation program. Epoch 2 took place after a year of simulation training.
- In the intervention year there were 22 postpartum hemorrhage simulations performed involving greater than three hundred nursing and obstetrical and anesthesia providers at different stages of their training. This equates to roughly two trainings per month.
- A computerized obstetrical database included all women who delivered at the institution during this time period and was used for analyzing patient data surrounding the simulation trainings.
- Attending physicians were not involved intentionally to preserve the learning environment.
- Transfusion of blood products was chosen as a proxy for clinical performance, and estimated blood loss was chosen as a secondary outcome.

INTERVENTION (# IN THE GROUP): 165 (Epoch 2)

COMPARISON (# IN THE GROUP): 157 (Epoch 1)

FOLLOW UP PERIOD: One year

RESULTS:

Primary Outcome –

- Women treated by clinicians with simulation training received blood products significantly sooner in the first 12 hours following delivery compared with women treated by clinicians without training (51 vs 102 minutes; *P*=.005).

Secondary Outcome –

- Women treated by clinicians with simulation training had significantly lower estimated blood loss than women treated by clinicians without training (1,250 mL vs 1,500 mL; *P*=.032).

LIMITATIONS:

- Attending physicians were not used in the study as to preserve the learning environment. This was recognized as a weakness as postpartum hemorrhage events would always be attended by a faculty physician.

- Other additional personnel, including blood bank staff and surgical technologists were not included.
- The timing of the simulation coincided with the implementation of the Alliance for Innovation in Maternal Health Hemorrhage bundle statewide in Texas and at this institution. This may have skewed some of the already present baseline education of those partaking in the simulation.
- This was performed in a single center with many resources and may not be representative of other institutions with different patient populations or smaller volumes.

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Pediatric Post-Concussion Resumption of Physical Activity at 72 Hours

Is early activity resumption after paediatric concussion safe and does it reduce symptom burden at 2 weeks post injury? The Pediatric Concussion Assessment of Rest and Exertion (PedCARE) multicentre randomised clinical trial

Ledoux AA, Barrowman N, Bijelić V, et al. Is early activity resumption after paediatric concussion safe and does it reduce symptom burden at 2 weeks post injury? The Pediatric Concussion Assessment of Rest and Exertion (PedCARE) multicentre randomised clinical trial. *Br J Sports Med.* 2022; 56(5):271–278. doi:10.1136/bjsports-2021-105030

KEY TAKEAWAY: Resuming non-contact activity at 72 hours post pediatric concussion versus rest-until-asymptomatic is safe and may be associated with milder symptoms at two weeks follow up.

STUDY DESIGN: RCT

LEVEL OF EVIDENCE: STEP 2

BRIEF BACKGROUND INFORMATION: Current concussion consensus guidelines recommend 24-48 hours rest with symptom limited, stepwise resumption of physical activity (PA) after symptoms resolve. There is limited evidence and few trials showing that therapeutic PA resumption 72 hours post-concussion is associated with milder symptoms.

PATIENTS: Youth ages 10 to <18 years old with acute concussion

INTERVENTION: Four-week stepwise return-to-PA protocol at 72 hours post-concussion

CONTROL: Return-to-PA once asymptomatic

OUTCOME: Self-reported symptoms at two-weeks using Health and Behavior Inventory score

METHODS (BRIEF DESCRIPTION):

- Included patients aged 10 to <18 years old with acute concussion in Emergency Room (ER).
- Multicentered: Three ER sites
- Randomized to stepwise return-to-PA at 72 hours post-concussion vs return-to-PA once asymptomatic.
- In ER a baseline was obtained, Health and Behavior Inventory (HBI) out of 63 and Balance Error Scoring System (BESS).
- Participants and parents were given education, instructions, and an Actical accelerometer (an energy/activity and step count monitor to assess compliance with the protocol) worn for 14 days post-ER visit.
- Patients were followed for four weeks, contacted daily by phone or e-mail for 14 days to report physical activity, symptoms, and sleep/awake times.
- Follow up surveys included HBI and adverse events (AE) at one week, two weeks, and four weeks.

INTERVENTION (# IN THE GROUP): 227

COMPARISON (# IN THE GROUP): 229

FOLLOW UP PERIOD: Contacted daily for two weeks (Health and Behavior Inventory); followed for four weeks

RESULTS:

Compared to the control group (CG), post-concussive symptoms at two weeks did not differ significantly from the experimental group (EG).

- Mean HBI total symptom score (EG 15 vs CG 16; adjusted mean difference [MD] −1.3; 95% CI, −3.6 to 1.1)
- 16 participants (EG=7 and CG=9) had unscheduled and unrelated medical visits, with no protocol deviation. No AE recorded.
- Valid accelerometer data 259/456 (58%); with protocol adherence: EG=77/113 (68%), CG=89/146 (60%)
- EG had less symptoms based on the HBI score than CG (MD −4.3; 95% CI, 8.4 to −0.2)
- EG had no difference compared to CG in terms of increased symptoms (EG 6% vs CG 16%; MD −9.8%; 95% CI, −20 to 0.8).
- EG had no difference in delayed recovery (EG=4.5%, CG 12% (group difference = −7.5; 95% CI, −17 to 2.1; NNT 13).

LIMITATIONS:

- No objective biomarker to diagnose concussion.
- Potential sampling bias for more severe concussions because patients were collected from the ER.
- Low accelerometer data 259/456 (58%) showed low protocol adherence; experimental group 68% and control group 60%.
- Unable to generalize results to younger children.

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The opinions and assertions contained herein are those of the authors and are not to be construed as official or as reflecting the views of the US Army Medical Department, the Army at large, or the Department of Defense.

Breaking Convention: Fosfomycin for MDR *E. coli* Treatment?

Effectiveness of Fosfomycin for the Treatment of Multidrug-Resistant Escherichia coli Bacteremic Urinary Tract Infections: A Randomized Clinical Trial

Sojo-Dorado J, López-Hernández I, Rosso-Fernandez C, et al. Effectiveness of Fosfomycin for the Treatment of Multidrug-Resistant Escherichia coli Bacteremic Urinary Tract Infections: A Randomized Clinical Trial. *JAMA Netw Open*. 2022; 5(1):e2137277. Published 2022 Jan 4. doi:10.1001/jamanetworkopen.2021.37277

KEY TAKEAWAY: Fosfomycin was less effective than ceftriaxone/meropenem in treatment of bacteremic Urinary Tract Infections (bUTI) because it led to more discontinuations due to adverse events. Fosfomycin may still be effective in healthy younger (<80 years old) patients lacking heart/renal insufficiency.

STUDY DESIGN: Multicenter, open-label randomized clinical trial

LEVEL OF EVIDENCE: STEP 2

BRIEF BACKGROUND INFORMATION: Overprescription of broad-spectrum antibiotics has resulted in an increase in multidrug-resistant (MDR) bacteria. As a result, treatment of bUTI caused by MDR *E. coli* has proved challenging given that the first line antibiotics are no longer effective. This study evaluates the use of fosfomycin as an alternative antibiotic option for bUTI treatment.

PATIENTS: Adult patients with bUTI caused by MDR *E. coli*

INTERVENTION: IV fosfomycin followed by oral fosfomycin

CONTROL: IV ceftriaxone/meropenem followed by comparable oral antibiotic

OUTCOME: Clinical and microbiological cure assessed in modified intention-to-treat population (MITT; received at least 1 study drug).

Secondary Outcome: Length of hospital stay; relapses or reinfections; 60-day mortality. These were assessed in clinically evaluable population (CEP; patients with previous failure at end of treatment) and microbiologically evaluable population (MEP; patients with urine cultures at end of treatment).

METHODS (BRIEF DESCRIPTION):

- Data was collected from hospitalized adult patients with bUTI caused by MDR *E. coli* demonstrating resistance to at least one drug of the three antibiotic families effective against wild type *E. coli.*
  - 143 participants were recruited for the study from 22 Spanish hospitals.
- In the fosfomycin group, patients received 4 g IV every six hours in 60 minutes of fosfomycin disodium for four days followed by oral fosfomycin trometamol at 3 g every 48 hours for the next 6-10 days.
- In the comparator group, patients received 1 g IV every 24 hours of ceftriaxone in 2-4 minutes or meropenem at 1 g IV every 8 hours in 15-30 minutes for four days followed by oral cefuroxime axetil, ciprofloxacin, amoxicillin-clavulanate, trimethoprim-sulfamethoxazole or parenteral ertapenem at standard dosing according to the bacterial strain susceptibility profile for the next 6-10 days.
- Clinical and microbiological cure, evidenced by cessation of symptoms and absence of causative *E. coli* from blood/urine, was evaluated 5-7 days following the completion of treatment (TOC).
- Noninferiority margin was 7%.

INTERVENTION (# IN THE GROUP): 70

COMPARISON (# IN THE GROUP): 73

FOLLOW UP PERIOD: 60 Days

RESULTS:

Primary Outcome –

- Fosfomycin was inferior to ceftriaxone/meropenem in reaching CMC (Risk Difference [RD] -9.4; 1-sided 95% CI, -22 to ∞).
- The fosfomycin group had comparable clinical and microbiological failure to the comparator group (RD -5.4; 1-sided 95% CI, -∞ to 4.9).

Secondary Outcome –

- In CEP patients, fosfomycin led to more frequent clinical cure (97% vs 90%) than ceftriaxone/meropenem (RD 6.6; 1-sided 95% CI, -0.2 to ∞).
- In MEP patients, the fosfomycin group demonstrated comparable microbiological cure to the comparator group (83% vs 86%; RD -2.7;1-sided 95% CI, -13 to ∞).

LIMITATIONS:

- Noninferiority margin was very strict.
- Lack of blinding may have influenced patient withdrawal from the study and delay of hospital discharge in the fosfomycin group.

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Nutrition-Focused Group Visits vs Conventional Diabetes Group Visits

Comparison of Group Medical Visits Combined With Intensive Weight Management vs Group Medical Visits Alone for Glycemia in Patients With Type 2 Diabetes: A Noninferiority Randomized Clinical Trial

Yancy WS Jr, Crowley MJ, Dar MS, et al. Comparison of Group Medical Visits Combined With Intensive Weight Management vs Group Medical Visits Alone for Glycemia in Patients With Type 2 Diabetes: A Noninferiority Randomized Clinical Trial. *JAMA Intern Med*. 2020; 180(1):70-79. doi:10.1001/jamainternmed.2019.4802

KEY TAKEAWAY: For patients with diabetes that attended group visits, intensive nutritional counseling showed comparable improvement in A1C to medication intensification, with greater weight loss and less hypoglycemia in the nutritional counseling group.

STUDY DESIGN: Randomized, non-blinded, noninferiority clinical trial

LEVEL OF EVIDENCE: STEP 2

BRIEF BACKGROUND INFORMATION: Group visits are a promising model for diabetes care in the primary care setting. Conventional medication intensification for glycemic control is associated with weight gain and hypoglycemia. This study examined the effect of weight-management focused group visits on A1C levels vs conventional group visits.

PATIENTS: Patients with uncontrolled type 2 diabetes enrolled in group medical visits

INTERVENTION: Nutrition-focused intensive weight management group visits (WM/GMV)

CONTROL: Conventional medication-intensification group visits (GMV)

OUTCOME: A1C at six months and one year

Secondary Outcome: Weight loss, hypoglycemic events, diabetes medication effect score

METHODS (BRIEF DESCRIPTION):

- 263 outpatients from two VA clinics in North Carolina with type 2 diabetes, A1C greater than 7.5% (mean 9.1%), and BMI greater than 27 were randomized to two arms.
- GMV arm (control) received nine group visits over 24 weeks focusing on diabetes-related topics and medication optimization.
- WM/GMV arm (intervention) received low-carb diet counseling with baseline medication reduction and 13 group visits over 24 weeks.
- WM/GMV dietician provided nutrition counseling on 20-30 g carb restriction without specific calorie restriction; classes covered meal makeovers, grocery shopping, and behavior change topics.
- Outcomes were measured at parallel time points in both groups. Laboratory measurements taken at baseline, 16, 32, and 48 weeks.
- Diabetes Medication Effect Score (DMES) reflects overall intensity of a diabetes regimen by consolidating dosage and potency of agents used. High-dose metformin provides a score of 1.5. With insulin and multiple other agents, a score of 7 or higher is possible.

INTERVENTION (# IN THE GROUP): 127

COMPARISON (# IN THE GROUP): 136

FOLLOW UP PERIOD: 48 Weeks

RESULTS:

Primary Outcome –

- There was no difference in A1C between WM/GMV and GMV (MD 0.1%, 95% CI, −0.5% to 0.2%).

Secondary Outcome –

- A1C improved without medication up-titration in the WM/GMV group (MD, −0.5; 95% CI, −0.6 to −0.3).
- Fewer hypoglycemic events were seen in the WM/GMV participants (incidence rate ratio, 0.49; 95% CI, 0.27–0.71).
- Weight loss was greater in the WM/GMV group (MD -3.7kg; 95% CI, −5.5 to −1.9 kg).
- Diabetic medication burden was significantly lower in the WM/GMV group (measured via DMES: estimated mean difference −0.5; 95% CI, −0.6 to −0.3).

LIMITATIONS:

- The intervention group had a higher frequency of visits during the first 16 weeks.
- Study physicians and participants could not be blinded to group assignment

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Empiric Vitamin D Supplementation Does Not Improve Overall Mortality Outcomes

Association between vitamin D supplementation and mortality: systematic review and meta-analysis

Zhang Y, Fang F, Tang J, et al. Association between vitamin D supplementation and mortality: systematic review and meta-analysis [published correction appears in BMJ. 2020 Sep 22; 370:m2329]. *BMJ.* 2019; 366:l4673. Published 2019 Aug 12. doi:10.1136/bmj.l4673

KEY TAKEAWAY: Empiric Vitamin D supplementation alone is not associated with a reduction in all-cause mortality compared with placebo or no treatment.

STUDY DESIGN: Systematic review and meta-analysis of 50 RCTs (N=74,655)

LEVEL OF EVIDENCE: STEP 1

BRIEF BACKGROUND INFORMATION: Vitamin D supplementation has been a large component of maintaining and/or improving musculoskeletal health. Observational studies have found that low Vitamin D status is associated with increased mortality from life threatening conditions such as cancer and cardiovascular disease. However, studies have been inconsistent and unreliable given the associated confounding variables such as supplementation with calcium.

PATIENTS: Adults with any health condition

INTERVENTION: Vitamin D administration

CONTROL: Placebo or no treatment

OUTCOME: All-cause mortality

Secondary Outcomes: Cancer mortality, cardiovascular mortality, non-cancer and non-cardiovascular mortality, cerebrovascular mortality, ischemic heart disease mortality

METHODS (BRIEF DESCRIPTION):

- Comprehensive literature review of RCTs with specific inclusion and exclusion criteria.
- Inclusion Criteria:
  - Adults 18 years and older with any health condition
  - Vitamin D supplementation vs placebo or no treatment (if receiving other agents, had to be at same dose for all the patients, i.e., calcium)
- Exclusion Criteria:
  - If patients were pregnant, critically ill, receiving hydroxylated, or vitamin D analogues

INTERVENTION (# IN THE GROUP): 37,535

- Vitamin D3: 28,813
- Vitamin D2: 8,722

COMPARISON (# IN THE GROUP): 37,120

FOLLOW UP PERIOD:

- 34/50 studies had a follow up of at least three years.
- 16/50 studies had a follow up of less than three years.

RESULTS:

Primary Outcome –

- Empiric vitamin D supplementation does not affect all-cause mortality (50 trials, N=74,655; RR 0.98; 95% CI, 0.95–1.0).

Secondary Outcome –

- Vitamin D supplementation significantly reduces cancer mortality (5 trials, N=39,197; RR 0.85; 95% CI, 0.74–0.97).
- No statistically significant difference between Vitamin D supplementation and placebo/no treatment regarding cardiovascular mortality, non-cancer, non-cardiovascular morality, risk of death from cerebrovascular disease, or ischemic heart disease.

LIMITATIONS:

- Most of the trials did allow for personal supplementation with low dose vitamin D which can make it difficult to appropriately distinguish between control and treatment group.
- The studies did not look at Vitamin D status and rushed independent isolation. Supplementation in the setting of status might imply different conclusions.

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