GEMs
GOOD EVIDENCE MATTERS

GEMs of the Week

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What's in this week's issue?

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SPOTLIGHT: Continuous Glucose Monitoring for Type II Diabetics without Prandial Insulin

Continuous Glucose Monitoring for Type II Diabetics without Prandial Insulin

GEMs GOOD EVIDENCE MATTERS SPOTLIGHT

Effect of Continuous Glucose Monitoring on Glycemic Control in Patients with Type 2 Diabetes Treated with Basal Insulin: A Randomized Clinical Trial

Martens T, Beck RW, Bailey R, et al. Effect of Continuous Glucose Monitoring on Glycemic Control in Patients with Type 2 Diabetes Treated with Basal Insulin: A Randomized Clinical Trial. *JAMA*. 2021; 325(22):2262–2272.

KEY TAKEAWAY: Adults with poorly controlled type II diabetes who are treated with basal insulin regimens have better diabetes control at eight months when using continuous glucose monitoring compared to standard blood glucose monitoring.

STUDY DESIGN: Multicenter, randomized, open-label, parallel-group clinical trial

LEVEL OF EVIDENCE: STEP 2

BRIEF BACKGROUND INFORMATION: Continuous glucose monitoring (CGM) has been shown to benefit patients with type II diabetes using intense insulin therapy (combination basal and prandial insulins). However, most adults with type II diabetes who are insulin dependent are on basal insulin alone. There have been no prior studies evaluating the utility of CGM in this population.

PATIENTS: Adults with type II diabetes treated with basal insulin

INTERVENTION: CGM

CONTROL: Traditional blood glucose meter monitoring

OUTCOME: HbA1c

Secondary Outcomes: Mean glucose level, time in target glucose range (70–180 mg/dL), and time with glucose >250 mg/dL

METHODS (BRIEF DESCRIPTION):

- Adults 30 years old or older with type II diabetes were included if they have been treated with 1 or 2 daily injections of long or intermediate-acting basal insulin at home for at least 6 months, had a HbA1c level between 7.8 and 11.5, self-reported blood glucose monitoring at least three times a week, and had availability of a smart phone.
- Prior to randomization, blood was drawn, patient heights and weights were measured, and diabetic education was provided.
- Participants were randomized into the following groups in a 2:1 ratio:
  - CGM: Blood glucose was measured every five minutes by the CGM, with additional metered monitoring performed by patients as needed.
  - Meter monitoring: Patients measured blood glucose fasting and postprandial 1 to 3 times daily.
- Patients were followed both clinically and virtually at 2 weeks, 1 month, 2 months, 4 months, 6 months, and 8 months.
- Primary and secondary outcomes were measured at 8 months.

INTERVENTION (# IN THE GROUP): 116

COMPARISON (# IN THE GROUP): 59

FOLLOW UP PERIOD: Eight months

RESULTS:

Primary Outcome –

- The CGM group had a greater decrease in HbA1c compared to the meter monitoring group (adjusted risk −0.4%; 95% CI, −0.8 to −0.1).

Secondary Outcomes –

- The CGM group had a significantly lower mean glucose level compared to the meter monitoring group (adjusted difference, –26 mg/dL; 95% CI, −41 to −12).
- The CGM group had a significantly greater time spent in the target blood glucose range compared to the meter monitoring group (adjusted difference, 15%; 95% CI, 8%–23%).
- The meter monitoring group had significantly greater time spent with a glucose >250 mg/dL compared to the CGM group (adjusted difference, −16%; 95% CI, −21% to −11%).

LIMITATIONS:

- All participants had increased contact with clinic staff due to their participation in the study.
- Participation was limited to those with CGM compatible smartphones, limiting generalizability.
- Participating primary care physicians received guidance from diabetes specialists which they would rarely receive in practice.
- Participants were not blinded to treatment given the nature of the intervention.

- Outcomes were measured up to eight months, limiting understanding of long-term effects.

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Can We Prevent Suicide with a Brief Acute Care Intervention?

Association of Suicide Prevention Interventions with Subsequent Suicide Attempts

Doupnik SK, Rudd B, Schmutte T, et al. Association of Suicide Prevention Interventions with Subsequent Suicide Attempts, Linkage to Follow-up Care, and Depression Symptoms for Acute Care Settings: A Systematic Review and Meta-analysis. *JAMA Psychiatry*. 2020; 77(10):1021–1030.

KEY TAKEAWAY: Brief suicide prevention interventions in an acute care setting may be effective in reducing the risk of subsequent suicide attempts and improving patients' odds of following up for outpatient mental health care.

STUDY DESIGN: Systematic review and meta-analysis of 14 RCTs (N=4,270)

LEVEL OF EVIDENCE: STEP 1

BRIEF BACKGROUND INFORMATION: When patients present to an acute care setting with suicidal ideation or a suicide attempt, resources need to be in place to prevent a future attempt. Outpatient follow up for mental health care is also of utmost importance for these patients to ensure appropriate treatment for depression.

PATIENTS: Adolescents and adults presenting to an acute care setting with suicidal ideation or a suicide attempt

INTERVENTION: Brief suicide prevention interventions

CONTROL: No intervention

OUTCOME: Subsequent suicide attempts and outpatient follow up

METHODS (BRIEF DESCRIPTION):

- Brief therapeutic interventions were defined as interventions aiming to prevent patients from engaging in future suicidal behaviors or promote ongoing mental health treatment engagement and were delivered to the patient during the single in-person encounter or in brief telephone calls.
- The most common brief therapeutic intervention was the Safety Planning Intervention.
- A subset of the studies was used in each meta-analysis.
- Suicide attempts and linkage to follow care were measured using validated self-report and medical record review.
- Odds ratio and Hedges' g standardized mean difference were used in determining effect size.

INTERVENTION (# IN THE GROUP): 2,241

COMPARISON (# IN THE GROUP): 2,029

FOLLOW UP PERIOD: 1 week to 12 months

RESULTS:

- Interventions decreased the risk of subsequent suicide attempts compared to no intervention (OR 0.7; 95% CI, 0.5–0.9).
- Brief interventions resulted in increased odds for outpatient follow up to occur (OR 2.7; 95% CI, 1.8–4.2).

LIMITATIONS:

- Literature search was limited to published studies and to English language only.
- Only 14 trials were included.
- Only a subset with relevant outcome was included in each meta-analysis.
- Did not examine if the intervention prevented death by suicide.
- One large study accounted for a large proportion of patients (n=1,376).

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Prevention of Postpartum Hemorrhage after Cesarean Delivery with IV Oxytocin: What is the Proper Dose?

Intravenous Oxytocin Dosing Regimens for Postpartum Hemorrhage Prevention Following Cesarean Delivery: A Systematic Review and Meta-Analysis

Phung L, Farrington E, Connolly M et al. Intravenous oxytocin dosing regimens for postpartum hemorrhage prevention following cesarean delivery: a systematic review and meta-analysis. *Am J Obstet Gynecol*. 2021; 225(3):250.e1-250.e38. doi:10.1016/j.ajog.2021.04.258

KEY TAKEAWAY: Bolus plus infusion regimen of intravenous (IV) oxytocin may be the preferred route of administration to reduce average blood loss in women undergoing cesarean delivery. For bolus only regimens, a dose of 10 IU may be superior to a dose of 5 IU, as it reduces need for additional uterotonics.

STUDY DESIGN: Systematic review of 26 comparative randomized control trials, 4 dose-finding randomized control trials, and 5 nonrandomized studies of interventions (N=7,333)

LEVEL OF EVIDENCE: STEP 1

BRIEF BACKGROUND INFORMATION: Throughout the world, postpartum hemorrhage is a major cause of maternal death. With uterine atony as the most common cause of postpartum hemorrhage, uterotonics such as IV oxytocin provide the opportunity to reduce morbidity and mortality in both vaginal and cesarean delivery. WHO guidelines lack evidence to recommend dosing regimens of oxytocin in prevention of postpartum hemorrhage after cesarean delivery.

PATIENTS: Women who gave birth via cesarean delivery

INTERVENTION: Intravenous oxytocin with various administration methods and dosages

CONTROL: Varied (administration method and dosages compared to each other)

OUTCOME: Incidence of postpartum hemorrhage ≥1,000 mL

Secondary Outcomes: Blood loss, uterine tone, use of additional uterotonics, and adverse maternal events

METHODS (BRIEF DESCRIPTION):

- Eligible studies included women who gave birth via cesarean delivery at any gestational age and received IV oxytocin for prevention of postpartum hemorrhage during or around the third stage of labor. This included both live and still births. This also included planned and intrapartum cesarean deliveries. To be eligible, studies had to compare at least two different dosing regimens of IV oxytocin.
- Intravenous oxytocin administered via bolus, infusion, or bolus plus infusion with varying doses were compared with and each other.
- Separate analyses were performed for the type of IV administration, total amount of oxytocin administered, and the effects of varying initial bolus doses (for studies with bolus plus infusion regimens).
    - Total oxytocin doses:
        - <5 IU vs 5-9 IU (145 women)
        - 5-9 IU vs 10-19 IU (177 women)
        - 5-9 IU vs 20-49 IU (2,996 women)
        - 10-19 IU vs 20-49 IU (331 women)
        - 20-49 IU vs ≥50 IU (180 women)
    - Initial bolus dose vs bolus plus infusion regimen:
        - <5 IU initial bolus vs 5 IU bolus plus infusion (180 women)
        - 5 IU initial bolus vs 10 IU bolus plus infusion (87 women)
- Adverse maternal events included nausea, vomiting, headaches, hypotension, etc.

INTERVENTION (# IN THE GROUP): 7,333

COMPARISON (# IN THE GROUP): Not applicable

FOLLOW UP PERIOD: Not available

RESULTS:

Primary Outcome –

- Bolus plus infusion regimen slightly decreased the mean blood loss compared to bolus only regimens (5 trials, N=3,068; mean difference [MD] 52 mL; 95% CI, 0.4–104 mL; moderate certainty).

Secondary Outcomes –

- Bolus plus infusion regimen increased the incidence of satisfactory uterine tone compared to bolus only regimens (1 trial, n=145; relative risk [RR] 0.63; 95% CI, 0.4–0.95; low certainty).
- An initial bolus dose of <5 IU reduced nausea compared to 5 IU in a bolus plus infusion regimen (3 trials, N=180; RR 0.29; 95% CI, 0.10–0.81; low certainty).
- This use of 10–19 IU demonstrates a large decrease in the use of additional uterotonics compared to the use of 5–9 IU (2 trials, N=137; RR 13; 95% CI, 1.8–96; low certainty).

LIMITATIONS:

- This study focused on comparisons between multiple different administration methods and doses of oxytocin rather than a common control. This makes it difficult to suggest one method and/or dose is superior to all others.

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Breastfeeding Practices: SARS-CoV-2 and Its Antibodies in the Breast Milk of Mothers Confirmed with COVID-19

Coronavirus Disease 2019 Vaccine Response in Pregnant and Lactating Women: A Cohort Study

Gray KJ, Bordt EA, Ateyo C, et al. Coronavirus Disease 2019 Vaccine Response in Pregnant and Lactating Women: A Cohort Study. *Am J Obstet Gynecol.* 2021; 225(3):303.e1-303.e17.

KEY TAKEAWAY: The immunological response from COVID-19 mRNA vaccines in pregnant, lactating, and nonpregnant women were similar.

STUDY DESIGN: Prospective cohort study

LEVEL OF EVIDENCE: STEP 3 (downgraded due to the use of local non-randomized sample)

BRIEF BACKGROUND INFORMATION: More pregnant women compared to nonpregnant women have needed hospitalizations, ICU admissions, or have died due to acute pulmonary infections secondary to COVID-19. This population was excluded from the initial COVID-19 vaccine trials due to safety concerns. Evidence is lacking to assess a sufficient immune response in pregnant females and subsequent transmission of immunity to infants.

PATIENTS: Pregnant, lactating, and reproductive-aged nonpregnant females

INTERVENTION: COVID-19 vaccination in pregnant and lactating women

CONTROL: Nonpregnant women either naturally infected or immunized

OUTCOME: Maternal antibody levels

Secondary Outcomes: Symptoms; presence of antibodies in umbilical cord blood and breast milk samples

METHODS (BRIEF DESCRIPTION):

- Eligibility criteria for participation included pregnant, breastfeeding, or nonpregnant females 18–45 years old who received the COVID-19 vaccine (Pfizer/BioNTech or Moderna/NIH).
- A questionnaire, which gave one point to each adverse effect, was utilized to formulate a symptom and reactogenicity score.
- Blood and breast milk were collected at:
  - Initial vaccination
  - Second vaccination
  - 2–6 weeks after second vaccination
  - Delivery in pregnant females who delivered during study period
- Umbilical cord blood was collected from pregnant women who delivered during study period.
- Stored sera from non-pregnant and previously SARS-CoV-2 infected pregnant females was used for comparison.
- Timing of vaccination in pregnant women:
  - First trimester: 11 women (13%)
  - Second trimester: 39 women (46%)
  - Third trimester: 34 (40%)
- 13 women delivered during the study period, of which 10 women had cord blood samples obtained post-delivery.

INTERVENTION (# IN THE GROUP): 131 (84 pregnant & 31 lactating)

COMPARISON (# IN THE GROUP): 53 (16 nonpregnant and immunized & 37 previously infected and pregnant)

FOLLOW UP PERIOD: 3.5 months

RESULTS:

Primary Outcome –

- Antibody levels were similar post-vaccination in all groups.
  - Pregnant: Median 5.6 (IQR 4.7–5.9)
  - Lactating: Median 5.7 (IQR 5.1–6.2)
  - Nonpregnant: Median 5.6 (IQR 4.8–6.0)
- Antibody levels were significantly higher in those with vaccines compared to those with natural infection (data provided via figure; *P*<.001).

Secondary Outcomes –

- All groups, similarly, had few symptoms after the first vaccination.
  - Pregnant: Median 2 (IQR 1–3)
  - Lactating: Median 3 (IQR 2–4)
  - Nonpregnant: Median 2.5 (IQR 1–4.5)
- 32% of pregnant women and 50% of nonpregnant women experienced fever or chills.
- Pregnant, lactating, and nonpregnant women all experienced high rises in IgM, IgA, and IgG after first vaccination.
- All umbilical cord blood and breast milk samples had vaccine-induced antibodies.
- There was no difference in neutralizing antibody titer levels between umbilical cord and maternal serum.

LIMITATIONS:

- Confidence intervals were not provided.
- This study focused on a specific population of healthcare workers from two medical facilities in

Boston, Massachusetts, which may not reflect the general population.
- Only 13 participants delivered during this time and maternal/neonate immunity could not be assessed over time.
- Antibody titers, not T-cell mediated immune responses were analyzed.

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