POEMs

Patient-Oriented Evidence That Matters

Early Treatment of Gestational Diabetes Is Modestly Beneficial for Neonatal and Maternal Outcomes

Clinical Question

Are early diagnosis and treatment of gestational diabetes mellitus (GDM) in high-risk patients beneficial for neonatal and maternal outcomes?

Bottom Line

This well-designed randomized controlled trial showed that screening pregnant patients at high risk for GDM in early pregnancy, and treating if positive, had modest benefits. A composite adverse neonatal outcome was reduced in the early treatment group (number needed to treat [NNT] = 18). Severe maternal perineal injury was also reduced in the early treatment group (NNT = 36). (Level of Evidence = 1b)

Synopsis

The study was an international, multisite randomized controlled trial of GDM in early pregnancy (i.e., before 20 weeks' gestation). It included pregnant patients between four weeks' and 19 6/7 weeks' gestation with one or more risk factors for GDM, including a previous diagnosis of GDM, body mass index greater than 30 kg per m^2, 40 years or older, a first-degree relative with diabetes, previous macrosomia, polycystic ovary syndrome, or non-European ancestry. Women 18 years and older were eligible for the study if a 75-mg, two-hour oral glucose tolerance test that was performed before 20 weeks' gestation showed any of the following: a fasting glucose level of 92 to 109 mg per dL (5.11 to 6.05 nmol per L), one-hour glucose level greater than 180 mg per dL (9.99 nmol per L), or two-hour glucose level of 153 to 199 mg per dL (8.49 to 11.04 nmol per L). Participants were randomized to receive immediate treatment (n = 406) or repeat oral glucose tolerance test at 24 to 28 weeks' gestation (n = 396 control patients). Among the control patients, 67% met the diagnostic criteria for GDM and were treated at that time. Management for GDM included education, dietary advice, instruction on how to monitor blood glucose, and standard pharmacologic treatment with metformin or insulin based on specific glycemic thresholds. The first primary outcome was a composite adverse neonatal outcome, including birth before 37 weeks' gestation, birth weight of 4,500 g or greater, birth trauma, neonatal respiratory distress during the first 24 hours after birth, phototherapy, stillbirth or neonatal death, or shoulder dystocia. An adverse neonatal outcome occurred in 24.9% of patients in the early treatment group and 30.5% in the control group (–5.6 percentage points; 95% CI, –10.1 to –1.2; $P = .02$; adjusted relative risk = 0.82; 95% CI, 0.68 to 0.98; NNT = 18). The primary maternal outcome was pregnancy-related hypertension, which did not differ between groups (10.6% vs. 9.9%; not significant). Patients with preexisting hypertension were excluded from that analysis. Multiple secondary outcomes were assessed for mothers and neonates, and only severe maternal perineal injury was significantly different between groups: 0.8% in the early treatment group and 3.6% in the control group (–2.8 percentage points; 95% CI, –4.1 to –1.5).

Study design: Randomized controlled trial (single-blinded)

Funding source: Government

Allocation: Concealed

Setting: Population-based

Reference: *Simmons D, Immanuel J, Hague WM, et al.; TOBOGM Research Group. Treatment of gestational diabetes mellitus diagnosed early in pregnancy.* N Engl J Med. *2023;388(23):2132-2144.*

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Opioids Are Equal to Placebo in Adults With Acute Nonspecific Low Back or Neck Pain

Clinical Question

Are opioids effective in alleviating pain in adults with acute nonspecific low back or neck pain?

Bottom Line

In the rigorously conducted study, from week to week over a six-week period, adults with acute low back or neck pain treated with opioids had similar pain relief as those treated with placebo. (Level of Evidence = 1b)

Synopsis

The researchers recruited adults with less than 12 weeks of new-onset low back or neck pain who sought care from their primary care physician or in an emergency department. The patients could have radicular symptoms, but no alarm symptoms, and they had to have pain of at least moderate severity. The authors randomized the patients to receive an opioid (oxycodone, 5 mg twice daily and naloxone, 2.5 mg, titratable to 10 mg of oxycodone; n = 174) or placebo (n = 172). The patients were treated until their pain score was 0 or 1 out of 10 for three consecutive days or for a maximum of six weeks. Although the researchers assessed the participants at two, four, six, 12, 26, and 52 weeks after enrollment, the primary outcome was pain on a 10-point visual analog scale at six weeks. At baseline, both groups had similar pain ratings (5.7 and 5.6, respectively). After six weeks, more participants dropped out of the opioid group (19%) than the placebo group (15%). The remaining participants in both groups improved by a similar degree (2.8 and 2.2, respectively). At no point during the 52-week follow-up did patients treated with opioids experience more pain relief than patients treated with placebo. At a few points in time, patients treated with placebo had greater pain relief. The masking of participants worked—roughly one-half in each group could not guess their treatment assignment. Approximately one-third of participants in each group experienced adverse events, but serious adverse events were infrequent (4% and 2%, respectively). In pain studies, a change of 2 points on a 10-point scale is generally considered to be clinically meaningful. The study reported only average changes and did not report the proportion of participants in each group who achieved this threshold, thereby leaving the question of whether some patients respond better to opioids than others unanswered.

Study design: Randomized controlled trial (double-blinded)

Funding source: Government

Allocation: Concealed

Setting: Outpatient (any)

Reference: *Jones CMP, Day RO, Koes BW, et al.; OPAL Investigators Coordinators. Opioid analgesia for acute low back pain and neck pain (the OPAL trial): a randomised placebo-controlled trial [published correction appears in* Lancet. *2023;402(10402):612].* Lancet. *2023;402(10398):304-312.*

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Terbinafine, 250 mg Once Daily—12 Weeks on, 12 Weeks off, Four Weeks on—Is Preferred for Onychomycosis in Adults

Clinical Question

What is the best oral monotherapy for toenail onychomycosis in adults?

Bottom Line

Based on effectiveness, safety, and cost, a regimen of terbinafine, 250 mg once daily for 12 weeks, followed by a 12-week period of no therapy and then a four-week booster, was preferred for onychomycosis in adults for the outcome of complete cure at one year. This POEM aligns with the Canadian Dermatology Association's Choosing Wisely Canada recommendation: Do not prescribe systemic antifungals for suspected onychomycosis without mycologic confirmation of dermatophyte infection. (Level of Evidence = 1a–)

Synopsis

The goal of the network meta-analysis was to compare individual oral antifungal regimens directly and indirectly for onychomycosis in adults. The surface under the cumulative ranking curve (SUCRA), a measure of the likelihood that a regimen was more likely to be effective or to cause harms, was calculated for each study and outcome. The researchers identified a total of 21 studies. Study quality was mixed, with many studies failing to mask participants and/or physicians. An overall assessment of the quality of each study was not provided, although most were at moderate to

high risk of bias. The highest complete cure rates at one year were found with terbinafine, 250 mg once daily for 12 weeks, followed by no treatment for 12 weeks and then terbinafine, 250 mg once daily for another four weeks (SUCRA = 82.7%); the same regimen, but with an initial treatment period of eight weeks (SUCRA = 80.4%); and albaconazole, 400 mg once weekly for 36 weeks (SUCRA = 80.4%). Terbinafine, 250 mg once daily for 24 weeks, had the highest likelihood of mycologic cure (SUCRA = 92.4%). Terbinafine, 250 mg daily for 12 weeks, was found to be significantly safer than albaconazole, 400 mg weekly for 36 weeks; oteseconazole (Vivjoa), 600 mg daily for two weeks, then 600 mg weekly for 10 weeks; fluconazole, 300 mg once weekly for 12 months; and posaconazole (Noxafil), 200 mg daily for 24 weeks. The price of terbinafine is low compared with that of newer agents such as albaconazole and posaconazole.

Study design: Meta-analysis (randomized controlled trials)

Funding source: Self-funded or unfunded

Setting: Outpatient (any)

Reference: *Gupta AK, Venkataraman M, Bamimore MA. Relative impact of traditional vs. newer oral antifungals for dermatophyte toenail onychomycosis: a network meta-analysis study.* Br J Dermatol. *2023;189(1):12-22.*

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Nearly Zero Risk of Sexually Transmitting HIV When Viral Loads Are Less Than 1,000 Copies per mL

Clinical Question

What is the risk of sexually transmitting HIV when viral loads are less than 1,000 copies per mL?

Bottom Line

Among the disparate studies, when viral load was less than 1,000 copies per mL, there was nearly no chance of sexually transmitting HIV. (Level of Evidence = 2a)

Synopsis

The authors searched multiple databases, conference proceedings, and registries to identify studies that evaluated sexual transmission of HIV among serodiscordant couples. They ultimately included eight studies with 7,762 serodiscordant couples from 25 countries. The authors report that the studies overall were at low risk of bias. Because the studies were different (one cross-sectional study, one case-control study, three cohort studies, one analysis of the placebo arm in a randomized trial, and two randomized trials), the authors chose not to pool the data. In three studies, when the viral load was less than 200 copies per mL, no sexual transmission of HIV occurred. Four studies identified 323 cases of transmission, none of which occurred in partners who were considered to be adequately suppressed with antiretroviral therapy. In two studies, 81% and 92% of the transmissions occurred when the viral loads exceeded 10,000 copies per mL. The authors identified only two cases of transmission when the viral load was less than 1,000 copies per mL.

Study design: Systematic review

Funding source: Foundation

Setting: Outpatient (any)

Reference: *Broyles LN, Luo R, Boeras D, et al. The risk of sexual transmission of HIV in individuals with low-level HIV viraemia: a systematic review.* Lancet. *2023;402(10400):464-471.*

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