Cochrane for Clinicians

Putting Evidence into Practice

Mechanical Methods of Induction of Labor

Drew C. Baird, MD, FAAFP, and Skyler Brown, DO
Carl R. Darnall Army Medical Center, Fort Hood, Texas

Author disclosure: No relevant financial affiliations.

Clinical Question

Are mechanical methods of induction of labor safe and effective in the third trimester?

Evidence-Based Answer

Mechanical induction of labor with single or double balloon catheters is similar to induction with vaginal prostaglandin E2 (PGE_2; also known as dinoprostone [Cervidil, Prostin E2]) in rates of vaginal delivery achieved within 24 hours, and it has a more favorable safety profile (21 fewer uterine tachysystole events per 1,000 deliveries). Mechanical induction also decreases serious neonatal morbidity and perinatal mortality compared with PGE_2 (relative risk [RR] = 0.48). (Strength of Recommendation [SOR]: A, based on consistent, good-quality patient-oriented evidence.)

Balloon catheters reduce the risk of cesarean delivery compared with oxytocin (Pitocin; 126 fewer cesarean deliveries per 1,000 deliveries). (SOR: A, based on consistent, good-quality patient-oriented evidence.) There is no difference in neonatal or maternal morbidity or mortality between the two groups; vaginal delivery rates have not been appreciably compared.

Compared with low-dose vaginal misoprostol (Cytotec; 50 mcg or less every four or more hours), balloon catheters increase the risk of cesarean delivery (53 more cesarean deliveries per 1,000 deliveries), reduce the risk of uterine tachysystole (22 fewer events per 1,000 deliveries), and do not demonstrate a difference in rates of vaginal delivery achieved within 24 hours.[1] (SOR: A, based on consistent, good-quality patient-oriented evidence.)

Practice Pointers

Induction of labor is a common obstetric procedure, occurring in approximately 20% of deliveries in the United States.[1,2] Mechanical methods of induction of labor have been used for centuries, although their popularity decreased in the 1970s with the introduction of pharmacologic methods.[1,2] More recently there has been a resurgence in the use of mechanical methods because they are generally considered safer than pharmacologic methods.[2] This Cochrane review sought to determine the effectiveness and safety of mechanical methods of induction of labor in women beyond 24 weeks' gestation vs. pharmacologic methods and amniotomy.[1]

The review included 113 randomized controlled trials conducted on six continents involving a total of 22,373 women scheduled for induction of labor after 24 weeks' gestation.[1] Most studies included nulliparous and multiparous women beyond 37 weeks' gestation with intact membranes. Most studies excluded women with ruptured membranes, those with a previous cesarean delivery, and those at less than 37 weeks' gestation (19 of 113 studies had a minimal gestational age of 24 to 36 weeks for inclusion criteria). Mechanical methods reviewed included transcervical single or double balloon catheter, Laminaria tent inserted into the cervical canal, or extra-amniotic saline infusion. These were compared with vaginal or oral PGE_2, low-dose vaginal or oral misoprostol, intravenous oxytocin, or amniotomy; comparisons of single vs. double balloon catheters were also included. Primary outcomes were vaginal delivery achieved within 24 hours, uterine tachysystole, progression to cesarean delivery, and serious neonatal morbidity or mortality (e.g., seizures, birth asphyxia, neonatal encephalopathy, childhood disability) or serious maternal morbidity or mortality (e.g., uterine rupture, intensive care unit admission, sepsis). Overall, the evidence was considered very low to moderate in quality, blinding was not possible given the nature of the interventions, and there was variable bias risk.[1]

Compared with vaginal PGE_2, balloon catheters (single or double) reduced the risk of uterine tachysystole (RR = 0.35; 95% CI, 0.18 to 0.67; six studies; 1,966 women), amounting to 21 fewer incidents per 1,000 deliveries. Balloon catheters also reduced the risk of serious neonatal morbidity or perinatal mortality (RR = 0.48; 95% CI, 0.25 to 0.93; eight studies; 2,757 women), although absolute event rates were low. There were no differences seen in the rates of vaginal delivery achieved within 24 hours, cesarean delivery, or serious maternal morbidity or mortality.[1]

Compared with low-dose vaginal misoprostol, balloon catheters reduced the risk of uterine tachysystole (RR = 0.39; 95% CI, 0.18 to 0.85; eight studies; 1,322 women), equating to 22 fewer incidents per 1,000 deliveries. However, they also increased the risk of cesarean delivery (RR = 1.28;

These are summaries of reviews from the Cochrane Library.

This series is coordinated by Corey D. Fogleman, MD, assistant medical editor.

A collection of Cochrane for Clinicians published in *AFP* is available at https://www.aafp.org/afp/cochrane.

CME **This clinical** content conforms to AAFP criteria for CME. See CME Quiz on page 523.

95% CI, 1.02 to 1.60; 12 studies; 1,756 women) by 53 more cesareans per 1,000 deliveries. Between the two induction methods, there were no differences in vaginal delivery achieved within 24 hours or serious neonatal or maternal morbidity or mortality.[1]

Balloon catheters demonstrated inferiority to low-dose oral misoprostol in several outcomes. Balloon catheters increased the risk of vaginal delivery not achieved within 24 hours (RR = 1.28; 95% CI, 1.13 to 1.46; two studies; 782 women), meaning 133 more vaginal deliveries extending beyond 24 hours in 1,000 deliveries. Balloon catheters also slightly increased the risk of cesarean delivery (RR = 1.17; 95% CI, 1.04 to 1.32; seven studies; 3,178 women), resulting in an increase of 37 more cesarean deliveries per 1,000 deliveries compared with low-dose misoprostol. There were no differences in other primary outcomes.[1]

Compared with intravenous oxytocin, balloon catheters reduced the risk of cesarean delivery (RR = 0.68; 95% CI, 0.56 to 0.83; eight studies; 781 women), which would result in 126 fewer cesarean deliveries per 1,000 deliveries. This reduction was not seen in women with a previous cesarean delivery on subgroup analysis of studies that included women with previous cesarean deliveries. There were no other reported differences in primary outcomes.

No outcome differences were identified for balloon catheter vs. amniotomy or for single balloon catheter vs. double balloon catheter. Laminaria tents decreased the risk of uterine tachysystole compared with vaginal PGE_2 (RR = 0.11; 95% CI, 0.02 to 0.60; three studies; 188 women), with a net decrease of 118 incidents per 1,000 deliveries. Compared with vaginal PGE_2, extra-amniotic saline infusion increased the delay of vaginal delivery beyond 24 hours (RR = 1.74; 95% CI, 1.21 to 2.49; one study; 109 women).[1] Regarding studies of combined induction methods, the only significant difference demonstrated was that a single balloon catheter combined with cervical PGE_2 increased the rate of vaginal delivery achieved within 24 hours (RR = 0.32; 95% CI, 0.12 to 0.82; one study; 127 women) compared with low-dose vaginal misoprostol alone.[1]

These findings are consistent with guidance from the American College of Obstetricians and Gynecologists (ACOG), which supports the use of single balloon catheters as an acceptable alternative to pharmacologic methods, particularly in women with an unfavorable cervix. ACOG supports use of the Bishop pelvic scoring system to identify an unfavorable cervix (Bishop score of 6 or less), and recommends the use of cervical ripening agents such as mechanical cervical dilators in these patients. ACOG adds that Laminaria tents may be associated with an increased risk of infection.[3] The National Institute for Health and Care Excellence supports the use of double balloon catheters for induction of labor in women without a previous cesarean delivery, based on evidence regarding their safety and effectiveness.[4] Based on this Cochrane review, physicians can offer mechanical methods, such as single or double balloon catheters, for women in the third trimester with a medical indication for induction.

The practice recommendations in this activity are available at http://www.cochrane.org/CD001233.

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

References

1. de Vaan MDT, ten Eikelder MLG, Jozwiak M, et al. Mechanical methods for induction of labour. *Cochrane Database Syst Rev.* 2019;(10):CD001233.
2. Penfield CA, Wing DA. Labor induction techniques: which is the best? *Obstet Gynecol Clin North Am.* 2017;44(4):567-582.
3. American College of Obstetricians and Gynecologists Committee on Practice Bulletins—Obstetrics. ACOG Practice Bulletin no. 107: induction of labor. *Obstet Gynecol.* 2009;114(2 pt 1):386-397.
4. National Institute for Health and Care Excellence. Insertion of a double balloon catheter for induction of labour in pregnant women without previous caesarean section. Interventional procedures guidance (IPG528). July 23, 2015. Accessed January 22, 2020. https://www.nice.org.uk/guidance/ipg528/chapter/1-Recommendations

Metformin to Prevent Diabetes in Patients at Increased Risk

Alexis Reedy-Cooper, MD, MPH; Leesha Helm, MD, MPH; and David Lee, MD, Penn State College of Medicine, Hershey, Pennsylvania

Author disclosure: No relevant financial affiliations.

Clinical Question

In patients at increased risk of developing type 2 diabetes mellitus, is metformin effective for the prevention or delay of diabetes onset and its associated complications?

Evidence-Based Answer

In patients at increased risk of developing type 2 diabetes, metformin reduces the risk (number needed to treat [NNT] = 7; 95% CI, 6 to 10) compared with counseling on standard diet and exercise. Data are limited regarding adverse effects and long-term outcomes.[1] (Strength of Recommendation: B, based on inconsistent or limited-quality patient-oriented evidence.)

Practice Pointers

Patients with prediabetes, defined as impaired fasting glucose, impaired glucose tolerance, and/or an A1C of 5.7% to 6.4%, are at increased risk of developing type 2 diabetes. Type 2 diabetes has been associated with many complications, including neuropathy, retinopathy, cardiovascular disease, and kidney dysfunction.[1] According to the Centers

for Disease Control and Prevention, 13% of the U.S. population 18 years and older were diagnosed with type 2 diabetes in 2018.[2] From 2013 to 2016, 34.5% of the U.S. population 18 years and older were diagnosed with prediabetes[2]; 15% to 30% of these patients progress to type 2 diabetes within five years.[3]

The authors of this Cochrane review investigated whether metformin reduces the risk of type 2 diabetes in patients with prediabetes.[1] The review included 20 randomized controlled trials and 6,774 patients. The duration of intervention ranged from one to five years. The authors included trials that compared metformin with any pharmacologic intervention, behavioral intervention, placebo, or standard of care in populations with prediabetes. The primary outcomes of interest were all-cause mortality, incidence of type 2 diabetes, serious adverse effects, cardiovascular mortality, nonfatal myocardial infarction or stroke, health-related quality of life, and socioeconomic effects.

Patients who used metformin for one to five years were less likely to develop type 2 diabetes compared with patients counseled on standard (not intensive) diet and exercise (NNT = 7; 95% CI, 6 to 10). However, there was no significant reduction in the development of type 2 diabetes in patients taking metformin compared with those who were counseled on intensive diet and exercise. The Cochrane review did not define intensive vs. standard diet and exercise counseling. Additionally, there was no significant reduction in the development of type 2 diabetes in patients who were given metformin plus intensive diet and exercise counseling compared with patients who received only intensive diet and exercise counseling. Metformin ($220 to $1,177) was more expensive than the standard diet and exercise intervention ($61 to $184). However, the cost of the intensive diet and exercise intervention ($225 to $3,628) was higher than that of metformin.

This review had some limitations. Notably, 48% of the patients were from one study, and 60% of the reviews were conducted in a single country (China). The results were consistent across studies, although the results of some studies were not statistically significant. Importantly, there were limited data on mortality between treatment groups (complications were rare), as well as long-term outcomes.

A previous meta-analysis also found that metformin reduced the risk of developing diabetes (NNT = 14; 95% CI, 10 to 22).[4] Guidelines from the National Institute for Health and Care Excellence recommend metformin as an adjunct to intensive lifestyle modification or for patients incapable of lifestyle modification.[5] The American Diabetes Association recommends the use of metformin to reduce the risk of developing diabetes in high-risk individuals but suggests that it is inferior to lifestyle modifications.[6] It should be noted that within the United States, the cost of metformin is typically low. It is often included on the low-cost medication options at pharmacies for patients who need to pay out of pocket for their medications.

The practice recommendations in this activity are available at http://www.cochrane.org/CD008558.

Editor's Note: The numbers needed to treat and confidence intervals reported in this Cochrane for Clinicians were calculated by the authors based on raw data provided in the original Cochrane review.

References

1. Madsen KS, Chi Y, Metzendorf MI, et al. Metformin for prevention or delay of type 2 diabetes mellitus and its associated complications in persons at increased risk for the development of type 2 diabetes mellitus. *Cochrane Database Syst Rev.* 2019;(12):CD008558.
2. Centers for Disease Control and Prevention. National Diabetes Statistics Report, 2020. Accessed October 2, 2020. https://www.cdc.gov/diabetes/pdfs/data/statistics/national-diabetes-statistics-report.pdf
3. Centers for Disease Control and Prevention. Prediabetes: could it be you? 2014. Accessed February 14, 2020. https://stacks.cdc.gov/view/cdc/23481/cdc_232481_DS1.pdf
4. Barry E, Roberts S, Oke J, et al. Efficacy and effectiveness of screen and treat policies in prevention of type 2 diabetes: systematic review and meta-analysis of screening tests and interventions. *BMJ.* 2017;356:i6538.
5. National Institute for Health and Care Excellence. Type 2 diabetes: prevention in people at high risk. Public health guideline [PH38]. Updated September 15, 2017. Accessed February 14, 2020. https://www.nice.org.uk/guidance/ph38
6. American Diabetes Association. 5. Prevention or delay of type 2 diabetes: *Standards of Medical Care in Diabetes–2018*. *Diabetes Care.* 2018;41(suppl 1):S51-S54. ■