Comparative Effectiveness Review
Number 238

Cervical Ripening in the Outpatient Setting

Evidence Summary

Main Points

- The highest strength of evidence for outcomes of outpatient cervical ripening found in this report was low, with several important outcomes having insufficient evidence. A rating of low-strength evidence means that there is low certainty in the magnitude or direction of the findings, and that future studies could change the conclusions.
- Low-strength evidence suggested that outpatient cervical ripening with dinoprostone (intravaginal insert or intracervical gel) or single-balloon catheters (30–50 ml fill) were not significantly different for cesarean delivery, fetal/neonatal infection with dinoprostone and maternal infection, birth trauma or shoulder dystocia with single-balloon catheters in comparison with the same intervention in the inpatient setting.
- Low-strength evidence suggested that cesarean delivery and postpartum hemorrhage were not significantly different between cervical ripening with catheters (double-balloon or single-balloon) in the outpatient setting and dinoprostone in the inpatient setting.
- The evidence on outpatient cervical ripening with misoprostol, double-balloon catheters, or hygroscopic dilators was insufficient.
- Low-strength evidence suggested that the risk of cesarean delivery with dinoprostone intracervical gel 2.5 mg versus 5.0 mg, and with silicone versus latex single-balloon catheters in the outpatient setting was not significantly different. Evidence was insufficient to draw conclusions on other outcomes or other direct comparisons of interventions.

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- Low-strength evidence suggested that in the outpatient setting, the risk of cesarean delivery with prostaglandins was not significantly different than placebo, expectant management, and membrane sweeping. The incidence of meconium aspiration syndrome, shoulder dystocia, and uterine infection, primarily with dinoprostone, were not significantly different than placebo.
- There was no evidence comparing different mechanical methods with each other, with membrane sweeping or with expectant management in the outpatient setting.
- For all comparisons, there was insufficient evidence on time from admission to vaginal birth, perinatal mortality, fetal/neonatal intracranial or subgaleal hemorrhage, hypoxic-ischemic encephalopathy, and maternal hemorrhage requiring transfusion.
- Comparative evidence on fetal surveillance for cervical ripening with a prostaglandin was not found.

Background and Purpose

The purpose of this review is to assess the comparative effectiveness and potential harms of cervical ripening in the outpatient versus the inpatient setting. The intended audience includes the American College of Obstetricians and Gynecologists' guideline developers, clinicians who deliver neonates (e.g., obstetricians, nurse-midwives, family physicians), other personnel who administer and monitor cervical ripening, and health system policymakers. In addition to these clinical implications, we hope to inform the future research necessary to provide high-quality, evidence-based care to all pregnant women.

Methods

We employed methods consistent with those outlined in the Agency for Healthcare Research and Quality Evidence-based Practice Center Program methods guidance (https://effectivehealthcare.ahrq.gov/topics/cer-methods-guide/overview), and we describe these in the full report. Our searches covered publication dates up to July 2020.

Results

We included 40 mostly fair-quality studies (30 randomized controlled trials [RCTs], 10 cohort studies), with 9,618 women. The majority of the evidence (22 RCTs, 1 cohort study) pertained to the comparative effectiveness and harms of cervical ripening methods in the outpatient setting. Participants' mean age was 28.8 years, most were nulliparous, mean baseline Bishop score was 3.4, and gestational age was 40.6 weeks. Most studies excluded women with prior cesarean delivery, but few studies excluded women with diabetes or hypertension of any type. Post-term pregnancy was the most common reason for cervical ripening. Tables A–C summarize our findings; the full report provides more outcomes and details. If a prespecified, primary outcome is not listed in a table below that

means that no study reported on that outcome (e.g., time from admission to vaginal delivery) or the evidence was insufficient to draw conclusions (i.e., due to imprecise estimates [too few patients or events], lack of corroborating evidence [a single study], and study limitations). The highest strength of evidence found for any outcome was low strength. No studies that met inclusion criteria were identified which addressed the comparative effectiveness and harms of fetal surveillance for cervical ripening with a prostaglandin in any setting.

Table A. Primary birth outcome: cesarean delivery

Key Question	Intervention	Findings[a]	Studies	Incidence	Relative Risk (95% CI) I^2 for Pooled Analyses[b]
Key Question 1: Prostaglandin Outpatient vs. Inpatient	Dinoprostone outpatient vs. inpatient	Low-strength evidence of little or no difference	2 RCTs (n=1,120)	23% vs. 23%	RR 0.97 (0.75 to 1.25)
	Dinoprostone outpatient vs. inpatient	Low-strength evidence of little or no difference	4 cohort studies (n=2,511)	33% vs. 33%	RR 0.79 (0.67 to 0.98)
Key Question 2: Mechanical Method Outpatient vs. Inpatient	Single-balloon catheter outpatient vs. inpatient	Low-strength evidence of a small, but nonsignificant, difference	3 RCTs (n=370)	12% vs. 20%	RR 0.59 (0.21 to 1.03)
	Single-balloon catheter outpatient vs. inpatient	Low-strength evidence of a small, but nonsignificant, difference	2 cohort studies (n=1,057)	33% vs. 30%	RR 0.95 (0.72 to 1.22)
	Outpatient catheter vs. inpatient dinoprostone	Low-strength evidence of a small, but nonsignificant, difference	2 RCTs (n=549)	33% vs. 26%	RR 1.24 (0.88 to 1.70)
Key Question 3: Outpatient Comparison of Methods	Dinoprostone gel 2.5 mg vs. 5.0 mg	Low-strength evidence of little or no difference	1 RCT (n=116)	20% vs. 19%	RR 1.07 (0.51 to 2.22)
	Prostaglandin vs. placebo	Low-strength evidence of a small, but nonsignificant, difference	12 RCTs (n=924)	16% vs. 21%	RR 0.80 (0.58 to 1.09), I^2=4.3%
	Prostaglandin vs. expectant management	Low-strength evidence of little or no difference	4 RCTs (n=615)	27% vs. 26%	RR .95 (0.68 to 1.33)
	Dinoprostone vs. membrane sweeping	Low-strength evidence of a small, but nonsignificant, difference	3 RCTs (n=339)	22% vs. 15%	RR 1.44 (0.85 to 2.36)
	Silicone vs. latex single-balloon catheters	Low-strength evidence of little or no difference	1 RCT (n=534)	39% vs. 40%	RR 0.98 (0.80 to 1.22)

CI = confidence interval; RCT = randomized controlled trial; RR = relative risk

[a] Difference of < 5% = little or no difference; 5% to 10% = small difference; 11% to 20% = moderate difference; >20% = large difference.

[b] I^2=0% unless otherwise indicated.

Table B. Primary fetal harms outcomes

Key Question	Intervention	Outcome	Findings[a]	Studies	Incidence	Relative Risk (95% CI) I^2 for Pooled Analyses[b]
Key Question 1: Prostaglandin Outpatient vs. Inpatient	Dinoprostone outpatient vs. inpatient	Infection	Low-strength evidence of little or no difference	2 RCTs (n=1,120)	4% vs. 3%	RR 1.39 (0.67 to 3.03)
Key Question 2: Mechanical Method Outpatient vs. Inpatient	Single-balloon catheter outpatient vs. inpatient	Birth Trauma[c]	Low-strength evidence of little or no difference	1 RCT (n=129)	2% vs. 3%	RR 0.49 (0.05 to 5.30)
	Single-balloon catheter outpatient vs. inpatient	Shoulder dystocia	Low-strength evidence of a moderate, but nonsignificant, difference	1 RCT (n=129)	3% vs. 11%	RR 0.28 (0.06 to 1.30)
Key Question 3: Outpatient Comparison of Methods	Dinoprostone vs. placebo	Meconium Aspiration Syndrome[d]	Low-strength evidence of a small, but nonsignificant, difference	2 RCTs (n=134)	2% vs. 4%	RR 0.76 (0.03 to 22.33)
	Prostaglandins vs. placebo	Shoulder dystocia	Low-strength evidence of a small, but nonsignificant, difference	3 RCTs (n=270) 2 RCTs (n=150)	3% vs. 0.70% 6% vs. 1%	RD 0.01 (–0.02 to 0.04)[e] RR 3.40 (0.55 to 20.95)

CI = confidence interval; RCT = randomized controlled trial; RD = risk difference; RR = relative risk

[a] Difference of ≤1% = little or no difference; >1% to 3% = small difference; >3% to 8% = moderate difference; >8% = large difference

[b] I^2=0% unless otherwise indicated.

[c] There were 3 cases total (1 in the outpatient and 2 in the inpatient group) which included 1 case each of brachial plexus injury, cephalohematoma, and scalp laceration plus cephalohematoma; authors did not report which specific injuries occurred in which group)

[d] Neonatal intensive care unit admission required, not specified as the Syndrome

[e] RD analysis is presented because one RCT reported no events and would not be included in a RR analysis. Of note, one of the other two trials reported a higher proportion of neonates with shoulder dystocia in the dinoprostone group (7.0% vs. 2.1%), but there was also a difference in the proportion of neonates with birth weight >4000 gm in the dinoprostone group (33% vs. 15%).

Table C. Primary maternal harms outcomes

Key Question	Intervention	Outcome	Findings[a]	Studies	Incidence	Relative Risk (95% CI) I^2 for pooled analyses[b]
Key Question 2: Mechanical Method Outpatient vs. Inpatient	Single-balloon catheter outpatient vs. inpatient	Uterine Infection	Low-strength evidence of little or no difference	2 RCTs (n=259)	5% vs. 5%	RR 0.99 (0.31 to 3.19)
	Outpatient catheter vs. inpatient dinoprostone	Postpartum Hemorrhage	Low-strength evidence of a small, but nonsignificant, difference	2 RCTs (n=549)	28% vs. 25%	RR 1.10 (0.62 to 1.56)

Key Question	Intervention	Outcome	Findings[a]	Studies	Incidence	Relative Risk (95% CI) I^2 for pooled analyses[b]
Key Question 3: Outpatient Comparison of Methods	Prostaglandins vs. placebo	Uterine Infection	Low-strength evidence of a small, but nonsignificant, difference	7 RCTs (n=771)	7% vs. 10%	RR 0.75 (0.40 to 1.39)
	Prostaglandins vs. expected management	Uterine Infection	Low-strength evidence of little or no difference	1 RCT (n=294)	6% vs. 5%	RR 1.21 (0.45 to 3.24)
	Prostaglandins vs. membrane sweeping	Uterine Infection	Low-strength evidence of a small, but nonsignificant, difference	2 RCTs (n=269)	7% vs. 4%	RR 1.22 (0.56 to 2.75)

CI = confidence interval; RCT = randomized controlled trial; RR = relative risk

[a] Difference of ≤1% = little or no difference; >1% to 3% = small difference; >3% to 8% = moderate difference; >8% = large difference

[b] I^2=0% unless otherwise indicated.

Strengths and Limitations

The evidence comparing interventions in the outpatient and inpatient settings suffers from too few RCTs with too small of sample sizes (range 48 to 827; mean 172), particularly when assessing harms that are rare. Evidence quantity and quality is low for specific interventions. These are: (1) misoprostol and double-balloon catheters (comparing each in the outpatient versus inpatient settings), (2) direct comparisons of single- and double-balloon catheters and catheters versus prostaglandins, (3) hygroscopic dilators, and (4) the various formulations and routes of administration of dinoprostone or misoprostol. These studies enrolled narrowly defined populations and did not analyze effects in important subgroups such as women over 30 or 35, Group B Streptococcus (GBS) status, diabetes, hypertension, fetal growth restriction, and gestational age categories. The studies generally either excluded women with such characteristics or failed to report on them in detail. There was variation in outcome definition and reporting across the studies, with many reporting outcomes not defined as specified in the protocol for this review. Differences in rare harms, such as hypoxic-ischemic encephalopathy, would require much larger studies (i.e., statistical power) than are currently available.

Implications and Conclusions

This report can inform guidance for clinicians and pregnant women on the relative benefits and harms of outpatient cervical ripening. This report found low strength of evidence that outpatient cervical ripening with dinoprostone and single-balloon catheters does not impose increased risk of cesarean delivery. We also found no indications of important signals of increased risk of fetal/neonatal and maternal harms, although not all such harms were adequately studied. The evidence is most applicable to younger women with singleton, vertex presentation pregnancies and low or no obstetric or medical risk factors. It does not identify the characteristics of pregnant women and fetuses that will benefit most or have the lowest risk of harm. There is evidence that women prefer, and

were satisfied with, outpatient cervical ripening, although the decision-making process is complex. Filling the gaps in the evidence will require RCTs with sample sizes large enough to evaluate important harms; that evaluate important subgroups of the population; and study outpatient misoprostol, double-balloon catheters. Observational studies should be prospective and use appropriate methods to control for confounding and effect modification.

Full Report

McDonagh M, Skelly AC, Hermesch A, Tilden E, Brodt ED, Dana T, Ramirez S, Fu R, Kantner SN, Hsu F, Hart E. Cervical Ripening in the Outpatient Setting. Comparative Effectiveness Review No. 238. (Prepared by the Pacific Northwest Evidence-based Practice Center under Contract No. 290-2015-00009-I for the Agency for Healthcare Research and Quality and the Patient-Centered Outcomes Research Institute.) AHRQ Publication No. 21-EHC011. PCORI Publication No. 2020-SR-03. Rockville, MD: Agency for Healthcare Research and Quality; March 2021.
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