Clinical Insights for Cervical Ripening and Labor Induction Using Prostaglandins

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Am J Perinatol Rep 2018;8:e307–e314.

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Abstract

Cervical ripening is often the first component of labor induction and is used to facilitate the softening and thinning of the cervix in preparation for labor. Common methods used for cervical ripening include both mechanical (e.g., Foley or Cook catheters) and pharmacologic (e.g., prostaglandins) methods. The choice of method(s) for ripening should take into account the patient's medical and obstetric history, clinical characteristics, and risk of adverse effects if uterine tachysystole were to occur. In this narrative review, we highlight the differences between the prostaglandins dinoprostone and misoprostol with respect to pharmacology and pharmacokinetics, efficacy, and potential safety concerns. Practical guidance on choosing an appropriate prostaglandin agent for cervical ripening and labor induction is provided via the use of clinical vignettes. Considering the advantages and disadvantages of each preparation allows clinicians to individualize treatment, depending on the indications for induction and unique characteristics of each patient.

Keywords

- prostaglandins
- dinoprostone
- misoprostol
- cervical ripening
- labor induction

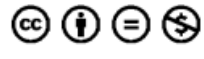
Labor induction is a common procedure that occurs in nearly 25% of term pregnancies.[1,2] In patients presenting with an unfavorable cervix, cervical ripening is the first component of labor induction and involves a series of complex biochemical processes leading to a multitude of changes, including rearrangement and realignment of collagen fibrils, changes in glycosaminoglycan composition, increased cytokine production, and white blood cell infiltration.[3–5] These changes facilitate the softening and thinning of the cervix, making the cervix ready for labor.

Cervical ripeness, as determined by Bishop's score (or one of its many modifications), is usually dichotomized into "favorable" or "unfavorable." Cervical ripening, whether endogenous or as the first step of a labor induction, results in improved efficacy of exogenous oxytocin, which is administered to stimulate uterine contractions.[6] Before initiating cervical ripening and labor induction, assessment of gestational age and potential risks to the mother or fetus are important. Key indications for labor induction include hypertensive disorders of pregnancy (e.g., preeclampsia), maternal medical conditions (e.g., chronic hypertension, diabetes mellitus), premature rupture of membranes (PROM), chorioamnionitis, placental abruption, fetal conditions (e.g., fetal growth restriction, oligohydramnios), and postterm pregnancy.[3,7] Labor inductions may also be performed electively for nonmedical reasons.[8]

The choice of method(s) for cervical ripening should take into consideration the patient's medical and obstetric history, clinical characteristics, and risk of adverse effects if tachysystole were to occur. The National Institutes of Child Health and Human Development (NICHD) definition of tachysystole is more than five contractions in 10 minutes, averaged over 30 minutes.[9,10] Different methods of cervical ripening may be preferred for different patients, and combination approaches are often utilized.[11] Common approaches for cervical ripening include both mechanical methods (e.g., Foley or Cook catheters) and pharmacologic methods (e.g., prostaglandins).[3,12] While mechanical methods, particularly Foley catheters, may be preferable in terms of cost and reduced risk of uterine

received
June 4, 2018
accepted after revision
September 11, 2018

DOI https://doi.org/10.1055/s-0038-1675351.
ISSN 2157-6998.



tachysystole, they must be placed by a physician who may not always be readily available on the labor and delivery unit.[13] Mechanical methods are associated with a learning curve for placement resulting in occasional failed placement.[13] Also, patients may experience mild to moderate discomfort with placement.[14] Pharmacologic methods (i.e., the prostaglandin preparations dinoprostone and misoprostol) provide alternatives to mechanical methods and may be preferred in many settings. Prostaglandins, which are naturally produced in the cervix and uterus, serve as mediators of cervical ripening,[15] and the administration of exogenous prostaglandin preparations leads to activation of collagenase, remodeling of the extracellular matrix, and generation of uterine contractions.[16] Although effective, prostaglandin preparations are associated with variable outcomes and risks of adverse effects based on the activities of the specific prostaglandins that they include. Similar to mechanical methods of cervical ripening, different prostaglandin preparations may be more difficult to dose vaginally than others. For example, it is recommended that dinoprostone gel be administered by a physician in a hospital setting[17] and misoprostol tablets need to be cut prior to administration which can lead to inaccurate dosing.[18,19]

This narrative review focuses primarily on pharmacologic methods of cervical ripening and labor induction, highlighting the differences between the prostaglandin preparations dinoprostone and misoprostol. Practical guidance on choosing the appropriate agent for cervical ripening and labor induction is provided via the use of clinical vignettes. Guidance regarding the choice of mechanical versus pharmacologic agents or single-agent versus combined approaches is largely beyond the scope of this manuscript.

Pharmacologic Prostaglandins for Cervical Ripening and Labor Induction

The body produces several prostaglandins that act through different receptor subtypes, each of which has distinct biochemical properties and signaling pathways (►**Fig. 1**). There are four subtypes of the E prostanoid (EP1–EP4) receptor; in general, EP1 and EP3 mediate contractility, and EP2 and EP4 mediate relaxation of the myometrium.[15,20] Prostaglandins may bind to multiple EP receptors, and with different affinities, resulting in effects that reflect a combination of the EP receptor activities. Through numerous studies, the presence of prostaglandin receptors EP1 through EP4 on uterine smooth muscle cells has been confirmed, and their role in labor has been well documented.[21,22]

Dinoprostone is chemically identical to endogenous prostaglandin E2 (PGE2) and is approved by the United States Food and Drug Administration (U.S., FDA) for cervical ripening; it is available as a vaginal insert (Cervidil, Ferring Pharmaceuticals Inc, Parsippany, NJ) or a cervical gel (Prepidil, Pfizer Inc, New York, NY). Both dinoprostone formulations require cold storage for chemical stability.[17,23] Compared with the cervical gel, the vaginal insert provides a more gradual increase in PGE2 levels and a longer duration of action,[19] releasing dinoprostone at a rate of 0.3 mg/hour for 12 hours.[23] In addition, the gel should be administered by a physician,[17] whereas the insert is easier to place and can be removed quickly, if needed.[19,24] A systematic review and meta-analysis of seven randomized controlled trials found that the dinoprostone vaginal insert was associated with a lower rate of cesarean deliveries and less oxytocin use in

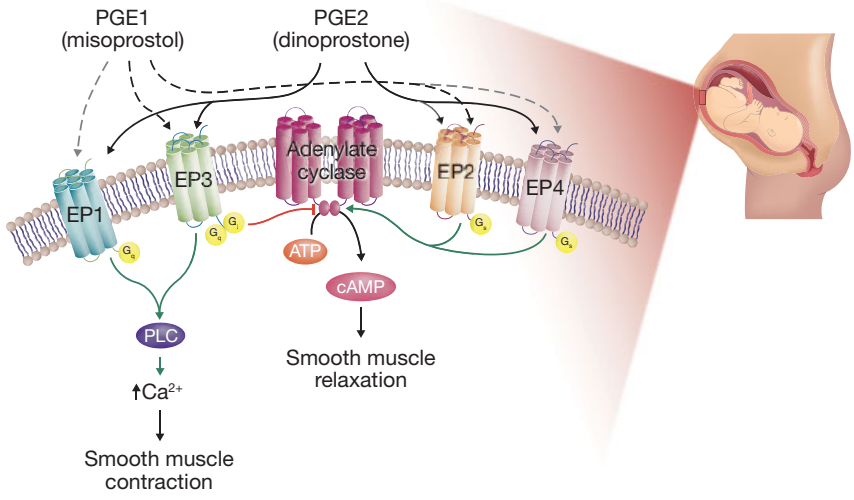


Fig. 1 Effect of prostaglandins on smooth muscle cells according to receptor subtypes. Abbreviations: ATP, adenosine triphosphate; cAMP, cyclic adenosine monophosphate; EP, E prostanoid; PGE, prostaglandin E; PLC, phospholipase C.

nulliparous women compared with repeated administration of vaginal or intracervical dinoprostone gel.[25]

Misoprostol is a synthetic analog of PGE1 that is approved by the U.S., FDA for prevention and treatment of gastrointestinal ulcers and peptic ulcer disease[26] but it is also widely used off-label for cervical ripening, as well as for pregnancy termination before 28 weeks of gestation and for treatment of postpartum hemorrhage.[3,19] Administration routes include oral, rectal, sublingual, and vaginal; however, absorption is variable.[27] For labor induction, the tablets are taken orally or inserted vaginally. However, because the tablets were not designed for vaginal administration, absorption can be slow and is unpredictable.[19] Additionally, for administration vaginally at or near term, the tablets must be scored and divided into fragments to obtain the desired dose for cervical ripening, leading to imprecise dosing.[16,18] Misoprostol also cannot be discontinued/removed if uterine tachysystole and consequent fetal heart rate tracing abnormalities occur.[16] Compared with dinoprostone, misoprostol has the advantages of lower cost and, since it does not require refrigeration, a longer shelf life.[16,26]

Pharmacology/Mechanism of Action

PGE2 targets all four EP receptors, activating EP1 and EP3 to increase intracellular calcium, while EP2 and EP4 stimulate cyclic adenosine monophosphate (cAMP) production (►**Fig. 1**).[15,21] Cervical ripening with dinoprostone is therefore theoretically similar to endogenous cervical ripening prior to spontaneous labor. Misoprostol has relative selectivity for the EP3 receptor but also binds EP2 and stimulates the release of endogenous PGE2, resulting in cervical ripening and increased uterine contractility.[16,28–30] In vitro studies indicate that misoprostol increases myometrial contractility at lower doses than dinoprostone.[29,30] These findings may explain higher rates of tachysystole and uterine rupture with misoprostol and suggest that differences in the prostaglandin signaling pathways and receptor expression may have clinical implications.[29,30] Characteristics of the prostaglandins are summarized in ►**Table 1**.

Clinical Pharmacokinetics

Dinoprostone is rapidly metabolized, with a half-life of approximately 2.5 to 5 minutes.[15,23] Vaginal misoprostol is typically dosed at 25 mcg in every 3 to 6 hours for cervical ripening and induction of labor; however, misoprostol is only available as 100 or 200 mcg tablets and requires dividing tablets into multiple pieces which may contribute to imprecise dosing since it is impossible to reliably break a tablet into four or eight equal portions.[18] The bioavailability of misoprostol is increased 2 to 3-fold with vaginal versus oral administration. Additionally, although plasma concentrations initially increase more slowly with vaginal misoprostol, levels are prolonged with vaginal versus oral administration.[19,27] While endogenous prostaglandins undergo rapid metabolism, synthetic prostaglandin analogs (e.g., misoprostol) are chemically modified to maintain bioavailability for a longer duration.[19] In contrast to the short half-life of dinoprostone (2.5–5 minutes),[23] misoprostol has half-lives of approximately 20 to 40 minutes

Table 1 Characteristics of dinoprostone and misoprostol for cervical ripening and induction of labor

Characteristic	Dinoprostone	Misoprostol
Description	PGE2[17,23]	Synthetic PGE1 analog[26]
Formulation	• 10 mg vaginal insert placed in the posterior fornix[23]	• Tablet, 100 or 200 mcg[26]; administered vaginally or orally[10,16]
Dose	• 0.3 mg/h released over 12 h[23]	• 25–50 mcg vaginally, every 4–6 h[19] • 25–100 mcg orally, every 2–4 h[5,19]
Receptor binding	EP1, EP2, EP3, EP4[15]	EP3 (potent); possibly EP2[15]
Pharmacologic effects	• Induces cervical remodeling[15,46] • Inconsistent effects on uterine contractions; may be related to cervical ripening vs. direct myometrial effect[15] • Mild stimulation of the GI tract[17]	• Induces cervical remodeling[15,16] • Generation of uterine contractions[15,16] • Increased contractility vs. PGE2 • Decreases total myometrial collagen and connective tissue vs. PGE2[15] • Stimulates the GI tract and may stimulate the fetal gut, resulting in meconium-stained amniotic fluid[15,32]
Pharmacokinetics	• Half-life: 2.5–5 min[23]	• Half-life (oral): 20–40 min[26] • Half-life (vaginal): 60 min[16,19]
Adverse effects	• Tachysystole (vaginal insert: 2.0%; cervical gel: 6.6%)[17,23] • Chills/fever (vaginal insert: $<$ 1%; cervical gel: 1.4%)[15,17,23] • Diarrhea/vomiting/nausea (vaginal insert: $<$ 1%; cervical gel: 5.7%)[15,17,23]	• Tachysystole (vaginal: 16.6%; oral: 7.0%)[47,48] • Chills/fever ($\leq$ 5%)[7] • Diarrhea/abdominal pain/nausea ($\leq$ 5%; increased with oral administration)[7,15,19]
Cost	• Vaginal insert: approximately $215.00–250.00; cervical gel: approximately $315.00[7,49]	• Approximately $2.00[7,49]

Abbreviations: EP, E prostanoid; GI, gastrointestinal; PGE, prostaglandin E.

when dosed orally and 60 minutes when administered vaginally.[19,31]

Clinical Efficacy and Safety/Complications

In the 2010 Cochrane review of 38 clinical trials comparing vaginal misoprostol with placebo or other pharmacologic methods (primarily dinoprostone; preparation types: gel, $n = 14$; insert/pessary, $n = 9$; tablet, $n = 3$; other/unknown, $n = 13$) in a broad population of women undergoing induction, there was no difference in the rate of vaginal births, although misoprostol was associated with a higher rate of vaginal delivery in 24 hours.[32] Misoprostol was associated with reduced use of epidural analgesia and oxytocin augmentation but was also associated with more uterine tachysystole and meconium-stained amniotic fluid compared with vaginal dinoprostone.[32] Similar results were reported in the 2016 meta-analysis of studies conducted in a general population of women undergoing induction: there was no significant difference between vaginal misoprostol and vaginal dinoprostone in cesarean deliveries (risk ratio [RR]: 0.87; 95% confidence interval [CI]: 0.76–1.00), although, among women delivering vaginally, vaginal misoprostol was associated with significantly reduced risk of still being undelivered 24 hours after the start of labor induction (RR: 0.62; 95% CI: 0.49–0.79).[10] Significantly lower rates of uterine tachysystole with fetal heart rate changes were observed with vaginal dinoprostone compared with vaginal misoprostol (RR: 0.57; 95% CI: 0.36–0.88).[10] Consistent with these meta-analyses, vaginal delivery within 24 hours is a commonly reported efficacy endpoint in clinical trials. However, it is important to note that the goal of induction is a safe vaginal delivery, regardless of whether the delivery occurs within 24 hours.[33] Absence of uterine tachysystole and possibly absence of meconium-stained amniotic fluid would seem to be reasonable surrogate markers for a "safe" vaginal delivery. Fortunately, birth asphyxia due to labor management is an uncommon outcome and powering a study or meta-analysis for this outcome would require an extremely large sample size. Of note, the recent A Randomized Trial of Induction Versus Expectant Management (ARRIVE) trial comparing elective induction of labor at 39 weeks with expectant management in low-risk nulliparous women enrolled more than 6,000 patients to detect differences in a composite of several severe neonatal morbidity and perinatal mortality outcomes.[34]

As alluded to, most studies are not adequately powered to detect differences in rare or specific neonatal outcomes, even outcomes such as low Apgar scores and admissions to the neonatal intensive care unit (NICU), between the two prostaglandins and are often conducted in a general population of women undergoing induction for a variety of indications. No differences in neonatal outcomes (i.e., birth weight, 5-minute Apgar score < 7, umbilical artery pH, meconium-stained fluid, requirement for resuscitation or intubation, and NICU admission) were observed in the 2009 trial of 112 women who received either vaginal misoprostol or dinoprostone.[35] In a prospective randomized trial of vaginal misoprostol, vaginal dinoprostone, and cervical dinoprostone (N = 111), tachysystole was significantly more common with misoprostol but there were no differences between treatments in neonatal birth weight, Apgar scores, or cesarean delivery.[36] Similarly, a larger randomized controlled trial (N = 1,358) reported a higher incidence of tachysystole requiring intervention in patients receiving a vaginal misoprostol insert compared with the dinoprostone vaginal insert (13 vs. 4%); neonatal outcomes (Apgar scores, acidosis, encephalopathy, antibiotic use, NICU admission, and respiratory events) were similar with both treatments.[37] A retrospective cohort study (N = 119) that compared misoprostol and dinoprostone vaginal inserts reported few cases of umbilical artery pH < 7.1, umbilical artery base excess ≤ 12 mmol/L, or a 5-minute Apgar score < 7 (no differences between cohorts) and no cases of tachysystole.[38]

Table 2 Factors associated with an increased risk of uterine tachysystole[39]

Factor	Characteristics associated with tachysystole
Patient	• Younger maternal age • Nulliparity • Chronic hypertension • Smoking/alcohol/drug history
Pregnancy/delivery	• Preeclampsia • Oligohydramnios • Induction of labor (not elective) • Use of oxytocin • Use of misoprostol • Longer time in labor • Epidural

Uterine tachysystole is associated with abnormal fetal heart rate patterns and may lead to adverse neonatal outcomes. In a retrospective cohort study, several patient and pregnancy factors were shown to increase the risk of uterine tachysystole (►**Table 2**).[39] Multiparity and maternal age of 30 years and older were associated with a decreased risk of tachysystole in multivariate analysis.[39] In a post hoc analysis of the phase 3 Efficacy and Safety Study Comparing Misoprostol Vaginal Insert Versus Dinoprostone Vaginal Insert for Reducing Time to Vaginal Delivery (EXPEDITE) trial that enrolled a large, general population of women undergoing induction, the retrieval of misoprostol or dinoprostone vaginal inserts was assessed in cases of intrapartum adverse events, including uterine tachysystole with fetal heart rate involvement and subsequent maternal events.[31] The vaginal insert was removed due to intrapartum adverse events in 11.4% ($n = 77/678$) of women who received the experimental misoprostol vaginal insert and 4.0% ($n = 27/680$) of women who received the dinoprostone vaginal insert ($p < 0.001$). The incidence of tachysystole with fetal heart rate changes was 5.3% ($n = 36/678$) with the misoprostol insert and 1.2% ($n = 8/680$) with the dinoprostone insert. The median time to resolution of uterine tachysystole with fetal heart rate involvement after insert retrieval was 94.5 minutes with misoprostol versus 8.5 minutes with dinoprostone.[31]

Summary
Both dinoprostone and misoprostol are prostaglandins commonly used for cervical ripening and labor induction. Dinoprostone is identical to endogenous PGE2 and targets all four EP receptors,[15,21] resulting in a process of cervical ripening that is similar to that which occurs prior to spontaneous labor. Misoprostol is a synthetic analog of PGE1 that strongly binds to the EP3 receptor and may also have affinity for EP2, resulting in cervical ripening and uterine contractility.[16,28–30] While dinoprostone is rapidly metabolized (half-life of 2.5–5 minutes),[15,23] misoprostol is chemically modified for longer duration of action (half-lives of 20–40 minutes with oral administration and 60 minutes with vaginal administration).[19,31] Dinoprostone is available as a cervical gel or controlled-release vaginal insert; both preparations require cold storage to ensure stability.[17,23] Misoprostol is available in 100 or 200 mcg tablets that can be divided and administered orally or vaginally.[19] Misoprostol is less expensive than dinoprostone and does not require refrigeration.[16,26] In contrast to the dinoprostone vaginal insert, misoprostol cannot be discontinued or removed if complications occur (e.g., uterine tachysystole, abnormal fetal heart rate tracings).[16]

The differences in the pharmacologic and pharmacokinetic profiles of these two agents may have important clinical implications. Findings from clinical studies including a broad population of women undergoing labor induction suggest that vaginal misoprostol was associated with a higher rate of vaginal delivery within 24 hours compared with vaginal dinoprostone; however, overall rates of vaginal birth and cesarean delivery were similar between groups.[10,32] Compared with vaginal dinoprostone, vaginal misoprostol was associated with increased risk of uterine tachysystole with fetal heart rate changes which could potentially result in adverse neonatal outcomes.[10,32] No significant differences in neonatal outcomes, such as Apgar scores, umbilical artery pH, or admission to the NICU have been reported with vaginal misoprostol and dinoprostone[35–38]; however, most studies were not adequately powered to detect significant differences in these rare outcomes.

Clinical Vignettes to Help Guide Treatment Selection

Considering our experience and practice guidelines published by the American College of Obstetricians and Gynecologists (ACOG), we provide clinical vignettes next to illustrate patient and pregnancy-related characteristics used in determining the most appropriate pharmacologic treatment for cervical ripening.

Clinical Vignette 1

Patient A is a 35-year-old P2002 at 37 weeks who has been undergoing antenatal testing due to fetal growth restriction. On the last ultrasound examination, the biophysical profile was 8/8, but the umbilical artery Doppler systolic/diastolic ratio, formerly within normal limits, now is above the 95th percentile. The patient is sent for delivery. Her cervix is closed, 20% effaced, and the presenting vertex is at −3 station. The decision is made to proceed with induction of labor starting with a prostaglandin agent. What is the preferred method of cervical ripening for this patient?

Elevated umbilical artery Doppler systolic/diastolic ratio > 95th percentile is an early and sensitive predictor of poor perinatal outcomes, including fetal heart rate tracing abnormalities, low Apgar scores, and higher admission rates to the NICU.[40,41] *For this patient, we would recommend dinoprostone over misoprostol due to concerns about fetal intolerance to labor if tachysystole were to develop. Risk of tachysystole is the most important reason to choose dinoprostone over misoprostol, as misprostol is associated with a higher risk of uterine tachysystole with fetal heart rate changes in the general population of induced women.*[10,32] *The dinoprostone vaginal insert also can be easily and quickly removed if complications arise. In addition to dinoprostone, the Foley catheter would also be a reasonable option for this patient.*

Clinical Vignette 2

Patient B is a 29-year-old primigravida who presents at 38 weeks to the labor and delivery triage area with complaints of contractions. Despite two to three contractions in every 10 minutes, her cervix is closed, 40% effaced, and the presenting vertex is at −1 station. During her evaluation, it is noted that she has two blood pressure readings 4 hours apart that are in the 140 s/90 s mmHg. The decision is made to induce labor for gestational hypertension. What is the preferred method of cervical ripening for this patient?

For this patient, we would select dinoprostone over misoprostol due to concerns that in a patient already having uterine contractions, misoprostol would be even more likely to cause tachysystole. Due to the potent binding of misoprostol to EP3[28] *which is responsible for myometrial contractility,*[15,20] *misoprostol demonstrates increased contractility compared with dinoprostone. This increased contractility combined with the current contractions that the patient is already experiencing increases the patient's risk for tachysystole (see Vignette 1). Another option for labor induction in this patient would be the use of mechanical ripening with a Foley catheter concurrently with or followed by oxytocin, as both Foley catheters and oxytocin are associated with a relatively low risk of tachysystole and fetal heart rate changes.*[10,32]

Clinical Vignette 3

Patient C is a 32-year-old P0101 at 37 weeks with suboptimal control of pregestational diabetes who has a scheduled induction of labor. When she presents for her induction, the labor and delivery census is quite high. Her cervix is closed, 20% effaced, and the presenting vertex is at −2 station. Due to the indication for induction, the care team is reluctant to reschedule the induction. The decision is made to start cervical ripening off the labor and delivery floor (on the antepartum floor). What is the preferred method of cervical ripening for this patient?

In this situation, we would choose the Foley catheter without concurrent oxytocin, as mechanical methods are thought to be favored for cervical ripening in the outpatient setting.[3]

Another possible option would be dinoprostone but not misoprostol due to concerns about tachysystole with the latter agent in a patient who is not physically located in labor and delivery; the patient's location may not be properly equipped with staff who are experienced with this type of potential complication (see Vignette 1). However, the safety of dinoprostone in a setting other than the labor and delivery unit has yet to be clearly established.

Clinical Vignette 4

Patient D is a 29-year-old P2002 who presents at 40 weeks with a history of a cesarean delivery for breech presentation followed by a vaginal birth after cesarean. Delivery is indicated due to gestational hypertension. Her cervix is 1 cm dilated and 40% effaced, with the presenting vertex at −2 station. What is the preferred method of cervical ripening for this patient?

We would suggest cervical ripening via a mechanical method, such as a transcervical Foley catheter for this patient.[12] *Prostaglandins are contraindicated for cervical ripening in the setting of a prior cesarean delivery. In women with prior cesarean delivery or a history of another myometrial incision (e.g., myomectomy), misoprostol has been associated with an increased likelihood of uterine rupture and should be avoided in the third trimester.*[3,42] *Though not specifically evaluated in a similar study, the use of dinoprostone is similarly contraindicated due to risk of tachysystole and concern about a potential but unproven association with uterine rupture.*

Clinical Vignette 5

Patient E is a 28-year-old P2002 at 38 weeks who presents with PROM and rare contractions; however, she is not in labor. Induction of labor is indicated. What is the preferred method of cervical ripening for this patient?

In the setting of PROM, oxytocin is generally used for induction of labor.[3,43] *A systematic review of 61 studies (including more than 12,000 women) found that oxytocin infusion alone is a safe and effective method for labor induction.*[6] *In women with PROM, findings from a large randomized controlled trial (N = 5,041) demonstrated that rates of cesarean delivery and neonatal infection were similar with oxytocin and dinoprostone vaginal gel; however, the incidence of chorioamnionitis tended to be higher with dinoprostone gel versus oxytocin (6.2 vs. 4.0%).*[44] *Women who received oxytocin for labor induction had fewer digital vaginal examinations and shorter labors compared with women treated with dinoprostone which may have contributed to the increased incidence of chorioamnionitis with dinoprostone. A recent randomized controlled trial comparing the Foley catheter with concurrent oxytocin versus oxytocin alone in women with PROM reported that cervical ripening with the Foley catheter in addition to oxytocin did not shorten the time to delivery but significantly increased rates of chorioamnionitis compared with oxytocin alone (8 vs. 0%).*[45] *The number of vaginal examinations was similar between groups. The rate of fetal scalp electrode use was higher in the Foley catheter group versus the oxytocin group; however, this was not related to the higher rates of chorioamnionitis with the Foley catheter. Due to the increased risk of infection with prostaglandins and mechanical methods,*[43–45] *the use of oxytocin without cervical ripening is recommended for this patient.*

Clinical Vignette 6

Patient F is a 28-year-old P1001 who presents to the labor and delivery unit at 25 weeks with a history of cesarean delivery at term, now reporting decreased fetal movement for the last 2 days. She is found to have a fetal demise. Her examination shows that her cervix is closed, thick, and the presenting part is at −3 station. Can a prostaglandin be used for cervical induction in the setting of a previous cesarean delivery and current fetal demise?

According to ACOG practice guidelines, either labor induction or dilation and evacuation is appropriate based on patient preference and whether dilation and evacuation is an available option.[3] *Vaginal misoprostol appears to be the most efficient method of labor induction before 28 weeks of gestation; typical dosages are 200 to 400 mcg vaginally every 4 to 12 hours. In women with a prior uterine scar, this misoprostol dose does not appear to increase complications. Given this patient's gestational age, even if dilation and evacuation was available, we would recommend labor induction using misoprostol.*

Clinical Recommendations for the Practicing Obstetrician/Gynecologist

The goal of labor induction is to minimize the time to vaginal delivery without compromising maternal or fetal safety. It is important to counsel the patient on the rationale for labor induction, including the risks involved and alternatives that might be available (e.g., cesarean delivery if indicated or expectant management if labor induction is elective). A summary of clinical practice recommendations based on the 2009 ACOG practice bulletin and our experience is provided in ►**Table 3**.

Conclusion

Dinoprostone and misoprostol are prostaglandins that have been frequently used for cervical ripening and labor induction for many decades. While their exact mechanisms are still being elucidated, dinoprostone and misoprostol appear to exhibit different actions on EP receptors and myometrial contractility. Consideration of the potential differences in pharmacology and pharmacokinetics of these agents, including half-lives and EP receptor potency and affinity, is important when selecting the most appropriate method for cervical ripening and labor induction for a specific patient. Clinicians must balance the efficacy of prostaglandin preparations and potential safety concerns for both mother and fetus. Findings from studies enrolling a general population of induced women indicate that misoprostol is associated with an increased risk of uterine tachysystole and dinoprostone may be favored over misoprostol in patients at risk for this complication. Further adequately powered studies are needed to compare neonatal outcomes with dinoprostone

Table 3 Summary of clinical practice recommendations[3]

Patient/pregnancy factor	Recommendation
Risk of uterine tachysystole/ hyperstimulation	• Important factor in choosing pharmacologic agent (dinoprostone vs. misoprostol) for cervical ripening • Dinoprostone is recommended over misoprostol when there is an increased risk of uterine tachysystole or an increased risk of fetal heart rate tracing abnormalities if tachysystole occurs • Dinoprostone is also recommended over misoprostol in women already having uterine contractions but needing cervical ripening • Mechanical methods may be considered if a physician is available for placement • Mechanical methods should be used in cases where prostaglandins are contraindicated
Prior cesarean or major uterine surgery	• Cervical ripening with prostaglandins is contraindicated unless prior to the third trimester and the fetus has expired • Mechanical cervical dilation (e.g., Foley catheter) is recommended
Premature rupture of membranes	• Oxytocin without cervical ripening is recommended due to the potential increased risk of chorioamnionitis with prostaglandins or mechanical cervical dilation, and the lack of evidence of benefit to cervical ripening before oxytocin induction in this setting
Fetal death	• $<$ 28 wk of gestation, vaginal misoprostol appears most efficient (if induction of labor is elected over dilation and evacuation) • $\geq$ 28 wk of gestation, Foley catheter or misoprostol; Foley is preferred if prior cesarean delivery

and misoprostol. Although this review focuses on prostaglandin preparations, it is important to note that mechanical methods, such as the transcervical Foley catheter, are also good choices for cervical ripening for many patients. Considering the advantages and disadvantages specific to each method of cervical ripening and labor induction allows clinicians to individualize treatment for each patient depending on the indications for induction and unique characteristics of each patient.

Conflict of Interest

R.K.E. has received research support from and has served as a scientific advisor for Ferring Pharmaceuticals. S.P., R.B., and D.A.M. have nothing to disclose.

Acknowledgments

Medical writing and editorial assistance for the development of this manuscript were provided by Kimberly Fuller, PhD, of SciFluent Communications, and were financially supported by Ferring Pharmaceuticals, Inc.

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