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Review of Evidence-Based Methods for Successful Labor Induction

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Abstract

Induction of labor is increasingly a common component of the intrapartum care. Knowledge of the current evidence on methods of labor induction is an essential component of shared decision-making to determine which induction method meets an individual's medical needs and personal preferences. This article provides a review of the current research evidence on labor induction methods, including cervical ripening techniques and contraction stimulation techniques. Current evidence about expected duration of labor following induction, use of the Bishop score to guide induction, and guidance on the use of combination methods for induction are reviewed.

Precis:

This is a state of the science review of methods for induction of labor at term gestation.

Keywords

First stage of labor; intrapartum care; induction; amniotomy; transcervical catheter; oxytocin

MeSH terms include:

Pregnancy; Cervical Ripening; Labor; Induction

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CONFLICT OF INTEREST

The authors have no conflicts of interest to disclose.

INTRODUCTION

Induction of labor (IOL) is the artificial stimulation of cervical ripening and progressive uterine contractions to facilitate birth.[1, 2] Between 2007 and 2017, the percentage of people experiencing IOL increased by nearly 10%, with more than one in four (25.5%) having an IOL in 2017.[3] More frequent use of induction techniques is driven by increasing numbers of pregnant people with medical complications during pregnancy and use of elective IOL prior to 42 completed weeks.[4–7] In addition, there is renewed interest in elective IOL following the publication of the ARRIVE trial (A Randomized Trial of Induction Versus Expectant Management), which demonstrated benefits of IOL at 39 weeks' gestation on rates of cesarean birth and hypertensive disorders of pregnancy among low-risk, nulliparous women in some settings.[8]

Although findings of the ARRIVE trial have fueled conversations about routine IOL, the American College of Nurse-Midwives (ACNM) continues to recommend waiting for spontaneous onset of labor in the absence of complications.[5] There are wide variations in hospital rates of cesarean birth following IOL; ranging from 32% to 60% in California alone.[9] This considerable heterogeneity in IOL success supports the need for greater use of evidence to determine the ideal methods for cervical ripening and contraction stimulation. This article summarizes current research on IOL methods for low-risk people at term gestation.

To identify current evidence on methods used to induce labor, four bibliographic databases, Embase.com, PubMed, Web of Science Core Collection, and Scopus were searched using the following inclusion criteria: 1) publications in English language, 2) IOL at or beyond early term gestation (37 0/7 weeks gestational age[10]), and 3) original research, meta-analyses, or systematic reviews involving labor induction methods of membrane sweeping, prostaglandins, cervical ripening balloon [transcervical catheters], amniotomy, and synthetic oxytocin. Search dates ranged between January 1, 2015 and October 11, 2020, with focus on studies published in the past three years.

BACKGROUND

Once a pregnant person and their care provider opt for labor induction after a shared decision-making process, IOL typically includes cervical ripening (if needed) followed by stimulation of uterine contractions and subsequent management of latent and active phases of labor.[11–14] Optimal IOL management begins with an individualized assessment of each patient's degree of labor readiness using the Bishop score (Table 1).[15] The California Maternal Quality Collaborative (CMQCC) suggests that cervical ripening continue until a Bishop score that is 6 or higher for multiparous and 8 or higher for nulliparous people.[16] If cervical ripening is indicated, mechanical and/or pharmacological interventions can be used.[17]

The next stage of induction focuses on stimulation of uterine contractions to cause progressive cervical dilation.[2] During the latent phase, laboring people experience regular painful contractions which are sometimes accompanied by other symptoms including bloody

show, fluid loss, or gastrointestinal symptoms.[18] The latent phase of IOL is often not recognized as a distinct component of an IOL, possibly contributing to premature diagnosis of failed IOL. In a recent study of nulliparous people (N = 10,677) in the United States,[19] researchers defined latent phase during IOL as starting after successful cervical ripening, synthetic oxytocin initiation, and amniotomy and ending when the cervix was 5 centimeters dilated. That study found that 65.5% of the participants reached active labor by 6 hours and 96.4% achieved active labor after a 15-hour latent phase. Although maternal morbidities like postpartum hemorrhage and chorioamnionitis increased with longer latent phase (P <.001 for both), most adverse perinatal outcomes including shoulder dystocia (P = .258) and uterine artery pH < 7.0 (P =.268) were not seen more frequently in participants with longer latent phases.

When an IOL is successful, induction methods trigger and advance physiologic positive feedback loops that progress from latent to active phase labor. According to the Obstetric Care Consensus guidelines by the American College of Obstetricians and Gynecologists and the Society for Maternal-Fetal Medicine,[20] a failed IOL occurs when the laboring person has no cervical progression during the latent phase after oxytocin is administered for at least 12–18 hours in the presence of ruptured membranes.[20.19] When following these guidelines strictly, investigators recently found that failed IOL occurred in only 2.0% of nulliparous people (N=4123) having an IOL between 39 and 40 weeks' gestation in a large medical system.[21] Once the active phase of IOL begins, unplanned cesarean births are not classified as 'failed labor induction,' but are instead indicated based on existing labor diagnoses, including labor arrest or concerning fetal heart rate pattern.[20]

CERVICAL RIPENING

Cervical ripening methods addressed in this review include membrane sweeping, prostaglandins, cervical ripening balloon, and synthetic oxytocin (Table 2, Supporting Information: Appendix S1).

Sweeping Membranes

Sweeping membranes is an intervention wherein 1–2 gloved fingers are inserted through the cervical os in order to sweep or separate the amniotic membrane from the lower wall of the uterus.[22] Sweeping of fetal membranes causes an immediate increase in prostaglandin F_{2alpha} metabolites.[11] Inside the cervix, these prostaglandins degrade the extracellular matrix of collagen fibers, causing them to become loosely organized and pliable.[11, 23] Antepartum membrane stripping in people who are recto-vaginally colonized with GBS appears to be safe and does not adversely affect maternal or neonatal outcomes.[24, 25]

In a systematic review and metanalysis from 2019 (7, studies, N=2252 birthing individuals), membrane sweeping compared to expectant management promoted spontaneous labor (RR, 1.21; 95% CI, 1.13–1.28, $P \leq .001$) and reduced the need for IOL after 42 weeks' gestation (RR, 0.52, 95% CI, 0.41–0.67, $P \leq .001$) without increased maternal or fetal morbidity.[26] A 2020 Cochrane review showed similar promotion of spontaneous labor with membrane sweeping compared to expectant management (aRR 1.21; 95% CI 1.08–1.34, 17 studies, N=3170 participants).[22] Those reviewers also found that membrane sweeping compared to

expectant management did not increase the risk for cesarean birth, assisted vaginal birth, maternal death, serious morbidities, or neonatal death. Membranes can be swept serially, but this approach is not more efficacious than a single sweep performed after 38 weeks' gestation.[22, 26]

In addition, membrane sweeping can be used during IOL to shorten the time to birth. In a 2018 meta-analysis (4 trials, N=1377 participants), Liu et al. examined the influence of membrane sweeping during the first cervical exam with IOL on participants' chances of achieving vaginal birth within 48 hours.[27] All participants included in this study were induced using a similar combination of mechanical or pharmacological interventions, either with or without membrane sweeping for the control and comparison groups. Lui found an increase in spontaneous vaginal birth within 48 hours if IOL was initiated with membrane sweeping. However, parity influenced outcomes; for nulliparous participants there was a 32% increase in spontaneous vaginal birth within 48 hours (RR, 1.32; 95% CI, 1.18 – 1.48) with first-examination membrane sweeping, while there were no differences in rates of spontaneous vaginal birth in 48 hours in multiparous participants. No adverse maternal or neonatal outcomes were noted with membrane sweeping.[27] Thus, there appear to be advantages for pregnant people of having their membranes swept, both in terms of avoiding labor induction and for increasing the likelihood of spontaneous vaginal birth in the first two days of IOL when used to initiate induction in nulliparous people.

Prostaglandins

Prostaglandins soften the cervix and upregulate gene expression for various contraction-associated proteins (CAPs), such as receptors for oxytocin, $PGE_{2,}$and PGF_{2alpha}, which transform the uterine myometrium so that it can generate strong and synchronous contractions.[11, 28] Prostaglandins are also potent systemic mediators of inflammation and infection, leading to pyrexia among some people following their use during labor.[29, 30]

There are two types of prostaglandins frequently used for cervical ripening in the United States: a PGE_1 analogue (misoprostol) and a PGE_2 analogue (dinoprostone). The PGE_1 analogue, misoprostol (Cytotec), is used off-label for IOL, as it is not approved by the Food and Drug Administration (FDA) for this use.[31] Misoprostol is used for term IOL in a variety of different doses (25 mcg – 50 mcg) and routes (vaginal, buccal, oral), most often administered every 4–6 hours. It is inexpensive, approximately $2.00/dose, and has a long shelf-life, but dosing is inexact as tablets are scored and must be divided for some dosage regimens.[30] In contrast, the PGE_2 analogue dinoprostone is FDA-approved for cervical ripening and comes in several different commercial preparations which include Cervidil, a 10mg vaginal insert that is dosed once/12 hours and delivers 0.3mg/hr, or Prepidil, a 0.5mg/2.5mL cervical gel that is dosed every 6 hours.[30] Both require refrigeration for chemical stability and are expensive, approximately $200-$300/dose. Dinoprostone requires a skilled clinician for insertion and the vaginal insert (Cervidil) has the advantage of easy removal if tachysystole or other adverse effects occur.

Recent evidence quantifies physiologic variations in the uterine response to different prostaglandins during IOL that support shorter labor durations associated with misoprostol compared to dinoprostone.[32] Benalcazar-Parra et al. conducted a cohort study (N = 500)

that included low-risk nulliparous participants admitted to the hospital for cervical ripening and IOL. This study used uterine electrohysterogram (EHG) to compare uterine electrical contractile responses following the administration of prostaglandins. For those who had a vaginal birth, the contractile amplitude and pseudo-Montevideo units (defined as the total contractile energy present on the EHG within a 30-minute interval) increased above the participants' basal state 60 minutes after misoprostol (25 mcg vaginal) drug administration. By contrast, in participants receiving dinoprostone (10 mg, vaginal insert), it took three times as long, or 180 minutes, for the pseudo-Montevideo units to increase. Participants receiving misoprostol also had a shorter mean time to active labor than those using dinoprostone (mean 15.45 h [SD 8.02] vs 17.38 h [SD 8.83] respectively, $P = .017$), and a shorter mean time to vaginal birth (misoprostol 18.69 h [8.57 h]; dinoprostone 21.21 h [9.87 h], $P = .009$). There were no differences in cesarean birth, uterine hyperstimulation, or meconium-stained amniotic fluid between the women who received either type of prostaglandin.

The route, number of doses, and frequency of administration of misoprostol for term cervical ripening is variable based on institutional guidelines and/or provider preference, although vaginal dosing is most common and most widely studied.[33] In a 2018 RCT, Pimentel and colleagues (N=243)[34] compared the rate of vaginal birth within 24 hours between a single 25 mcg dose of misoprostol administered vaginally followed by oxytocin within 4–6 hours vs. repeated dosing of 25 mcg misoprostol administered vaginally every 4–6 hours (maximum 4 doses) followed by oxytocin as clinically indicated. They found that the single-dose regimen was associated with an increased rate of cesarean birth among all participants (35.8% vs 22.8%, $P=.034$), which was more significant among nulliparous people (49.3% vs. 28.6%, $P=.016$). In analyses that accounted for differences between participants and their other IOL processes, these researchers found that the single-dose misoprostol regimen was acceptable for IOL only in people whose Bishop score was greater than 4 after their first misoprostol dose, or who were multiparous. These findings support guidance from CMQCC that providers should avoid premature initiation of oxytocin during IOL and instead continue cervical ripening until a Bishop score of 6 or higher for multiparous and 8 or higher for nulliparous people.[16]

Although not yet widely available in the United States, misoprostol solution for oral use shows promise over vaginal dosing for avoiding cesarean birth. In a 2014 Cochrane review (N=1282)[35] Alfirevic and colleagues found that a 20–25 mcg oral solution of misoprostol was as effective as misoprostol used vaginally, dinoprostone, or oxytocin for vaginal birth within 24 hours, resulted in fewer cesarean births, and showed no difference in rates of uterine hyperstimulation with or without FHR changes. However, the dosing of misoprostol appears to be important when it is used orally. For example, in a 2017 RCT Rouzi and colleagues (N=146)[36] found that an hourly titrated oral dose of misoprostol (maximum 60 mcg/hour for up to 24 h) compared to a static oral dose of misoprostol (25 mcg used orally every 2 hours) was associated with increased rates of cesarean birth (RR 2.83, 95%, 1.18–6.77, $P = .02$), maternal pyrexia ($P = .03$), and meconium-stained fluid ($P = .05$).

Vaginal and buccal administration of misoprostol were compared for time to birth and rate of cesarean birth in a 2019 double blind, placebo controlled RCT of women at term

with intact membranes (N=300).[33] An initial dose of 25 mcg was administered followed by 50 mcg every 4–6 hours up to a maximum of 7 doses, as clinically indicated based on cervical ripeness. Vaginal compared to buccal administration of misoprostol resulted in shorter median duration of labor (20.1 h vs. 28.1 h, $P = .006$), fewer cesarean births for an indication of non-reassuring fetal status (3.3% vs. 9.5%, $P = .03$), and more vaginal births within 24 hours (58.6% vs 39.2%, $P = .001$). Importantly, this study was not designed to assess possible increased rates of chorioamnionitis with vaginal dosing of misoprostol, as all participants received vaginal examinations on the same schedule.

Thus, misoprostol used vaginally may be more optimal than buccal administration in people with intact membranes. However, oral solution misoprostol provides benefits through limiting vaginal exams and possibly decreasing cesarean birth rates. Misoprostol used orally or vaginally demonstrate advantages over dinoprostone with regard to shorter IOL duration without increasing rates of uterine hyperstimulation or meconium-stained amniotic fluid.

Cervical Ripening Balloon

A cervical balloon is a mechanical method used for cervical ripening. Mechanical methods of IOL work by softening and stretching the cervix, exposing endometrial decidual cells and stimulating the release of endogenous prostaglandins PGE_2 and PGF_{2alpha} locally and systemically.[37, 38] Two cervical balloon devices are commonly available for use: a single-balloon device (Foley catheter) and a double-balloon device (Cook catheter). LaJustica et al., 2018 noted no differences between these catheters with regard to effectiveness or major adverse maternal or neonatal outcomes.[39] However, single balloon catheters are 30–40 times cheaper ($1.12) compared to the double balloon Cook catheter ($39.33). Given that there are minimal differences in outcomes, the single balloon is often preferred.[40]

Key benefits of cervical balloons compared to prostaglandins are their localized action with few systemic side effects and their ability to be discontinued easily; for these reasons, cervical balloons are the primary cervical ripening method used in outpatient settings or among people undergoing a trial of labor after cesarean birth.[41–45] Outpatient cervical ripening for IOL can be used among select groups of people with term pregnancies, showing evidence of improved cost savings over inpatient cervical ripening.[46]

The results of several studies provide information about the optimal use of cervical balloons for IOL. Regarding the tension placed on the cervical balloon, Fruhman and colleagues conducted an RCT in 2017 (N=140)[47] to examine the time to birth in groups of participants with tension vs. without tension. All participants had a Bishop score of 6 or lower and received low dose oxytocin (maximum 6 mU/min) after catheter placement. Researchers found no differences in the median time to birth among participants with or without tension (16.2 h versus 16.9 h, $P = .814$) although the median time to cervical balloon expulsion was slightly shorter among participants in the tension group versus the non-tension group (2.6 h versus 4.6 h, $P < .001$).[47]

Another common difference between providers who use cervical balloons is the volume to which they fill the balloon. In a 2018 meta-analysis of 7 RCTs (N=1432), Schoen and colleagues found that higher balloon filling volume (30 mL versus 60 mL or 80 mL filling

volume) shortened IOL duration for participants by a mean difference of 1.97 hours (95% CI, −3.88 to −0.06, $P = .04$), although their study was underpowered to assess how parity might change the relationship between filling volume and IOL duration.[48]

Cervical balloons do not appear to increase laboring people's risk of infection compared to vaginally-administered prostaglandins. In a 2015 meta-analysis (26 RCTs, N=5563 participants), McMaster and colleagues found similar rates of intra-amniotic infection (RR, 0.96; 95% CI, 0.66 – 1.38), endometritis (RR, 1.03; 95% CI, 0.66–1.38), pooled maternal infections (RR, 0.95; 95% CI, 0.81–1.12) and neonatal infections (RR, 0.90; 95% CI, 0.58–1.39) when comparing prostaglandins administered vaginally to cervical balloon placement for cervical ripening.[49] Similarly, in a 2018 meta-analysis, Zhu and colleagues (8 RCTs, N=2390 participants) found no significant differences between vaginal dinoprostone and intracervical foley on maternal infection rate among nulliparous participants with intact membranes (RR 0.74, 95% CI, 0.51, 1.07).[50]

Although effective for cervical ripening, people using cervical balloons demonstrate differences in labor progression compared to people using prostaglandins for cervical ripening. For example, Tuuli and colleagues reported labor progress differences in participants using cervical balloons compared to misoprostol in an observational study.[51] Participants using cervical balloons dilated faster in early labor from 1 cm cervical dilatation to 4 cm cervical dilatation than did participants using misoprostol (median 3.4 h versus 5.6 h; $P < .01$). However, in later labor (4 cm −10 cm of cervical dilatation), participants dilated slower after using a cervical balloon for ripening, compared to participants who used misoprostol (median 6.3 h versus 3.6 h, $P < .01$). Thus, the transition to the active phase of labor seems to occur at less advanced cervical dilatation among people using misoprostol for cervical ripening (around 4 cm) compared to people using cervical balloons (after 6 cm).

Despite these differences in the pace of cervical dilation in early labor, the overall duration of labor induction does not appear to be lengthened with cervical balloons compared to misoprostol. These were the findings in the Tuuli study (balloons with 60 mL fill),[51] and also in a 2016 RCT by Levine and colleagues (N = 491),[44] who compared a variety of induction methods and found that the overall duration of IOL in participants receiving misoprostol was similar to participants using 30mL filled cervical balloon (median 17.6 h versus 17.7 h, $P < .001$). Cervical balloons (50mL fill) were actually more efficient than misoprostol (25mcg oral dose every 2 h) on the mean time to birth in another study of 7551 nulliparous people.[52]

In addition, cervical balloons appear to shorten labor duration compared to dinoprostone. For example, in a 2017 cohort study (N=7551) Wollman and colleagues found that labor duration following cervical ripening with a cervical balloon (50 mL fill) was on average, 7 hours shorter than dinoprostone in nulliparous participants (mean duration of labor 18.3 h versus 25.2 h; 95% CI, −7.6 to −6.3).[52] However, as seen in the studies that compared misoprostol to cervical balloons, balloon volume appears to have an influence on the duration of IOL. A 2018 meta-analysis (8 RCTs, N=2390 nulliparous participants) by Zhu and colleagues saw no significant differences in the induction to birth interval between cervical balloons with moderate fill volume (30mL) and dinoprostone inserts (mean

difference, 0.71 h; 95% CI, −2.50 to 3.91; $P = .67$).[50] Together, these findings suggest that cervical balloons demonstrate advantages over prostaglandins for term cervical ripening on labor duration. There is some evidence that generous fill volumes (60–80mL) may hasten cervical ripening and that cervical balloons provide a safe and effective non-pharmacologic option for cervical ripening.

Synthetic oxytocin for cervical ripening—In addition to its more frequent use to stimulate uterine contractions during the second phase of labor induction (see below), synthetic oxytocin infused as a 'low-dose' titration is sometimes used for cervical ripening. However, there is limited data showing effectiveness of oxytocin for cervical ripening compared to other methods in a general population. For women who had a prior cesarean for whom prostaglandins are contraindicated, oxytocin infusion compared to cervical balloons (50mL fill) for cervical ripening was associated with fewer vaginal births (37% vs 50% respectively, $P = .05$) but otherwise had no significant difference in neonatal or maternal outcomes (including uterine dehiscence) in a 2019 French RCT (N=204) by Sarreau et al.[53] In that study, oxytocin used alone for cervical ripening was more likely to end with vaginal birth in participants with higher initial Bishop scores (> 4).

For women with term prelabor rupture of membranes (PROM) and an unfavorable cervix, oxytocin is recommended over vaginal use of misoprostol to decrease the frequency of cervical examination and possibly the risk of intra-amniotic infection.[54] However, the relationship between vaginal misoprostol and subsequent maternal infection in the setting of PROM is poorly understood due to limitations in the research.[55] Intrapartum intra-amniotic infection is established to be directly related to an increased number of cervical examinations, thus limiting cervical assessment, particularly in the latent phase of the first stage of labor, and instead utilizing other signs of labor progress and time (hours) may be important. In facilities with access to misoprostol that can be used orally, risk of infection may be reduced while increasing the chance of successful cervical ripening, although there is little evidence comparing these methods for women who have PROM at term gestations.

Early administration of synthetic oxytocin infusions for contractile stimulation during IOL may predispose people to cesarean birth.[34] In their 2018 RCT (N=243) of single vs multiple doses of vaginal misoprostol, Pimentel et al. performed a secondary analysis to evaluate predictors of cesarean birth according to the participant's Bishop score when oxytocin was initiated. They found that the risk of cesarean birth was inversely related to Bishop score at the time of oxytocin initiation. Using Poisson regression, Bishop score of less than 4 was the most significant predictor of cesarean birth(OR, 0.47; 95% CI, 0.30 – 0.74; P=.001) followed by multiparity (OR 0.49; 95% CI, 0.3–0.85; P=.008). Body mass index at or above 30 kg/m^2, gestational age more than 41 weeks, misoprostol frequency of dosing, estimated fetal weight, and timing of amniotomy were not associated with a risk of cesarean birth. Thus, clinicians should avoid solo use of oxytocin for cervical ripening unless prostaglandins or cervical balloons are contraindicated, and delay initiation of oxytocin infusions during IOL until the Bishop score indicates that cervical ripening is complete as strategies to decrease their patient's risk of cesarean birth.

Combination Methods for Cervical Ripening

There is an expanding body of evidence supporting the use of combination methods during cervical ripening. In a recent meta-analysis (N= 15 RCT's, approximately 2000 participants) Ornat and colleagues found that combined treatment with misoprostol (oral or vaginal) and cervical balloon was associated with a shorter induction to birth interval than misoprostol alone (mean difference, −1.99 h; 95% CI, −3.42 to − 0.56).[56] Interestingly, they also found a lower rate of uterine hyperstimulation (RR, 0.39; 95% CI, 0.23 – 0.67) and fewer neonatal intensive care unit (NICU) admissions (RR, 0.75; 95% CI, 0.58 – 0.97) among participants using combination methods compared to misoprostol alone. Similarly, Levine and colleagues conducted a RCT (N=491) examining single agent (misoprostol 25 mcg per vagina every 3 h, cervical balloon with 30mL fill) vs combination cervical ripening methods (misoprostol + cervical balloon and oxytocin + cervical balloon), and found that all combination methods shortened the median time to birth compared to single agent methods (misoprostol + Foley, 13.1 h; Foley + oxytocin, 14.5 h; versus misoprostol only, 17.6 h or Foley only, 17.7 h, $P < 0.001$).[44]

There is also recent evidence that parity may influence the effectiveness of combination cervical ripening methods involving cervical balloons plus oxytocin. In a 2018 meta-analysis of 6 RCT's (N=1133 participants), Liu and colleagues compared 2 groups of participants: cervical balloon (30–60mL fill) followed by standard dose oxytocin for IOL or cervical balloon with simultaneous initiation of oxytocin.[50] They found that multiparous participants in both groups were equally likely to give birth within 24 hours. However, nulliparous participants using a cervical balloon with simultaneous synthetic oxytocin experienced a 32% increased likelihood of birth within 24 hours (RR, 1.32; 95% CI, 1.12–1.55) compared with nulliparous participants using the cervical balloon with the later addition of synthetic oxytocin. There were no differences in maternal or neonatal outcomes between the groups. These findings suggest that the combination of a cervical balloon plus misoprostol or oxytocin is a safe and effective method for cervical ripening for people and should especially be considered when caring for nulliparous women requiring cervical ripening.

STIMULATION OF UTERINE CONTRACTIONS

There are two common methods to stimulate contractions following cervical ripening: amniotomy and synthetic oxytocin (Supporting Information: Appendix S2). Amniotomy involves puncturing or tearing of the amnion and chorion to release the amniotic fluid. Synthetic oxytocin (Pitocin) is administered intravenously for labor induction.

Amniotomy.

Artificial rupture of membranes is often used during IOL in combination with other agents to stimulate uterine contractions. When performed after cervical ripening, amniotomy can release accumulated endogenous prostaglandins in the amniotic membrane forebag to nearby uterine decidual tissue, thereby dramatically heightening contractility and labor progression as they stimulate release of local prostaglandins and contraction associated proteins (CAPs) in a positive feedback manner.[11]

Recent research on amniotomy focuses on the optimal timing of this intervention during IOL. Bala et al. 2018 (N=150)[57] examined the use of amniotomy at the start of labor induction versus amniotomy 4–8 hours later among participants with a Bishop score of higher than 6. In this RCT, they found that amniotomy at the beginning of induction was associated with a reduced mean time to birth (7.4 h versus 11.7 h, $P = .000$), but a higher rate of cesarean birth (10.7% versus 2.7%, $P = .049$) compared to delayed amniotomy. The incidence of intraamniotic infection and neonatal infection were not assessed. Supporting these findings, Battarbee et al., 2020 conducted a secondary analysis of data from the Consortium on Safe Labor (N=15,525 term participants), finding an increased odds of cesarean birth after amniotomy if participants were less than 4 cm dilated at the time, compared to participants with artificial or spontaneous rupture at greater than or equal to 4 cm (aOR, 1.30; 95% CI, 1.12–1.50).[58] Interestingly, they also found a significantly increased step-wise risk of cesarean birth with early amniotomy compared to delayed amniotomy in people with BMIs at or above 30 kg/m^2. In contrast, De Vivo and colleagues published a meta-analysis in 2020 (N=1273 in 4 trials) that found a similar risk of cesarean birth associated with early amniotomy during IOL (defined as amniotomy after expulsion of a cervical catheter, greater than or equal to 3 cm dilatation, or a Bishop score of ≥ 5) compared to later rupture of membranes (31.1% vs 30.9%; RR, 1.05; 95% CI, 0.71 – 1.56).[59] Like the Battarbee[58] and Bala[57] studies, De Vivo also found shorter labor durations in the early amniotomy group of approximately 5 hours (interval from IOL onset to birth: weighted mean difference, −4.95 h; 95% CI, −8.12 to −1.78).[59]

Early amniotomy may advance labor process and shorten time to birth when used after moderate cervical ripening and in combination with oxytocin initiation, but the effect on cesarean birth rates is not consistent across studies. Women with increased BMI may not gain as much benefit in response to amniotomy compared with women with lower BMI—especially with early amniotomy. It is also not clear what degree of cervical dilatation at the time of amniotomy maximizes the benefit of amniotomy while best decreasing risk during IOL.

Synthetic Oxytocin

Once cervical ripening is complete, causing activation of the uterine oxytocin receptors,[60] use of synthetic oxytocin (Pitocin) is an effective method to increase the frequency, duration, and intensity of uterine contractions for progressive cervical dilation during the latent phase of IOL.[61] Induced labor may take longer to progress through the latent phase of the first stage compared to spontaneous labor, and this is important information to share with pregnant people and their support persons as anticipatory guidance. In a cohort study (N = 5388), Harper and colleagues found that people who were induced had significantly longer labor lengths (4–10 cm) compared to those with spontaneous labor, regardless of parity (nulliparous participants: median 5.5 hours [5th percentile 1.8h, 95th percentile 16.8h] IOL vs. median 3.8 hours [1.2h, 11.8h] spontaneous labor; multiparous participants, median 4.4 hours [1.2h, 16.2h] IOL vs. median 2.4 hours [0.6h, 8.8h] spontaneous labor).[62] Slower progression of induced labor in that study was especially pronounced prior to 6cm, regardless of parity. Duration of labor at each centimeter of dilatation in that study was computed after accounting for the influence of labor induction, augmentation, race, body

mass index at or above 30 kg/m^2, birth weight above 4000g, and Bishop score greater than 5, so some laboring people may have shorter or longer IOL durations.

As the laboring person moves from latent to the active phase of labor (≥ 5 cm dilatation), their body often produces more endogenous oxytocin.[61] For this reason, some studies have found that synthetic oxytocin may be discontinued in the active phase of IOL without impeding success.[63, 64] For example, investigators of a 2018 Cochrane review and metanalysis (10 studies, N=1,888) found that when oxytocin was discontinued for persons in active labor, the cesarean birth rate was decreased (RR, 0.69; 95% CI, 0.56–0.86, low-certainty), as was the risk of uterine tachysystole with abnormal FHR changes (RR 0.15; 95% CI, 0.05–0.46, moderate-level certainty) compared to continuing oxytocin infusion until birth or fetal intolerance of labor occurred.[64] Although discontinuing synthetic oxytocin increased the duration of the active phase labor by a mean of 26 minutes (CI, 5.28–45.87; $P = .01$), this outcome should be interpreted with caution due to imprecision of consistently identifying the onset of active labor. In a similar study by Saccone and colleagues (N=1538 births, 9 RCTs),[63] oxytocin discontinuation during active labor decreased the cesarean birth rate (9.3% versus 14.7%; RR, 0.64; 95% 95% CI, 0.48–0.87), reduced the risk of uterine tachysystole (6.2% vs 13.1%; RR 0.53; 95% 95% CI, 0.33–0.84), and slightly increased the duration of active phase labor by a mean of 27.7 minutes (95% CI, 3.94–51.36; $P = .02$). According to guidelines for the Saccone trials, participants without cervical change or adequate uterine contractions for 2 hours or more following oxytocin discontinuation had their oxytocin infusions restarted. Using these guidelines, 30% of participants required re-initiation of the oxytocin infusion.

Based on this evidence, providers can take advantage of the physiologic transition from latent to active phase labor by decreasing or stopping synthetic oxytocin titrations, thus reducing the potential for unnecessary treatment and either reducing or not effecting the cesarean birth rate. Nonetheless, even after thorough cervical ripening, stimulation of progressive cervical dilation during IOL with oxytocin requires more time than spontaneous labor; thus, providing anticipatory guidance of this fact to pregnant people and their support persons is an essential step in caring for people undergoing IOL.

The primary adverse effects of oxytocin are uterine tachysystole and fetal heart rate decelerations. Optimal oxytocin dose titration as well as use of maximum dose of synthetic oxytocin that best avoid these complications have not been established, based on the current literature. In spontaneous labor, endogenous oxytocin is released in pulsatile fashion, with increased pulse frequency as labor advances.[65] Baseline plasma concentrations of endogenous oxytocin during spontaneous labor have been found to be comparable to a synthetic oxytocin infusion rate of 5–10 mU/min,[66, 67] and a synthetic oxytocin rate of 11–13 mU/min has been identified as one in which most women will achieve adequate contractions and birth.[68] Investigators examining the pharmacokinetics of synthetic oxytocin have found an onset of action of 3–5 minutes and a half-life of 10–12 minutes following infusion initiation; thus 30–60 minutes are required to achieve steady state.[69] Importantly, plasma concentrations of oxytocin are twice the infusion rate (e.g. rate of 10 mU/min leads to a plasma concentration level of 20mU/min).[67] Moreover, the physiologic response to synthetic oxytocin is widely variable, based on the activity and actions of enzymes

and oxytocin receptors that are influenced by age, parity, gestational age, and other metabolic factors such as obesity.[70] Thus, different people can respond with widely different contraction profiles to the same infusion rate of oxytocin, even when Bishop scores are comparable. Therefore, close observation during synthetic oxytocin infusion is necessary to protect both the laboring person and their fetus from harm.

Recommendations from ACOG[2] and AWHONN[71] regarding how to increase oxytocin titrations over labor are based not on the pharmacokinetics (Table 3), but rather on standard dosing regimens cited in the research literature. Only limited research information is available guiding optimal oxytocin dosing regimens. In a 2014 Cochrane review (N= 9 trials with 2391 participants) comparing high-dose (defined as ≥ 100 mU oxytocin in the first 40 minutes, with ≥ 600 mU infused in the first two hours) versus low-dose oxytocin (defined as < 100 mU oxytocin in the first 40 minutes, with < 600 mU total in the first two hours), investigators saw no difference by dosing regimen in rate of cesarean birth, maternal morbidity, or neonatal morbidity.[72] However, high-dose oxytocin increased rates of uterine hyperstimulation (RR 1.86; 95% CI 1.55 – 2.25) compared to low-dose oxytocin. Those authors concluded that additional research was needed to fully consider maternal and fetal effects of high-dose oxytocin regimens. A 2019 retrospective study of nulliparous women induced at term (N=4,885) also compared outcomes based on oxytocin dosing regimen (high-dose regimen of 6.67 mU/min for first 30 min, increased by 6.67 mU/min every 30 min thereafter versus a low-dose regimen of 2 mU/min for the first 30 min, increased by 2 mU/min every 30 min thereafter).[73] Those authors found no difference by dosing regimen in rates of cesarean birth, operative vaginal birth, or neonatal outcomes when dosing regimens were compared, but increased rates of postpartum hemorrhage were associated with the low-dose regimen (estimated blood loss at least 1000 mL, 10.5% vs. 7.8%, $P < .001$). Thus, they concluded that either regimen was acceptable. However, this recommendation is based on weak evidence and is contrary to the pharmacologic principle of administering the lowest effective dose for the shortest duration. Thus, providers should consider a strategy of increasing oxytocin durations at a given rate before increasing the dose and individualizing titrations based on each person's desires and their uterine and fetal response.

CONCLUSION

Induction of labor is more common than in the past due to increased medical risks among patients and increased interest in elective IOL. To decrease the occurrence of failed induction, providers need to understand the current evidence about methods for IOL. When possible, providers should first encourage/ensure adequate cervical ripening to a Bishop score of 8 for nulliparous or 6 for parous people prior to initiating synthetic oxytocin. Findings from this review suggest the importance of anticipatory guidance for people undergoing IOL that they can expect significantly longer labor, regardless of parity, compared to spontaneous labor. Knowledge of the mechanism of action, effectiveness, and side effects of each method is valuable in shared decision-making discussions with people needing or desiring induction of labor.

Supplementary Material

Refer to Web version on PubMed Central for supplementary material.

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References

1. American College of Nurse-Midwives. Induction of labor: Position statement. J Midwifery Women's Health2017;62(4):509–10. [PubMed: 28703929]
2. ACOG Practice Bulletin No. 107: Induction of Labor. Obstet Gynecol2009;114(2 Pt 1):386–97. [PubMed: 19623003]
3. Martin JA, Hamilton BE, Osterman MJK, Driscoll AK, Drake P. Births: Final data for 2017. National vital statistics reports: From the Centers for Disease Control and Prevention2018;67(8):1–50.
4. Fridman M, Korst LM, Chow J, et al.Trends in maternal morbidity before and during pregnancy in California. Am J Public Health2014;104Suppl 1:S49–57. [PubMed: 24354836]
5. Supporting healthy and normal physiologic childbirth: A consensus statement by the American College of Nurse-Midwives, Midwives Alliance of North America, and the National Association of Certified Professional Midwives. J Midwifery Womens Health2012;57(5):529–32. [PubMed: 22954092]
6. Dublin S, Johnson KE, Walker RL, et al.Trends in elective labor induction for six United States health plans, 2001–2007. J Midwifery Women's Health2014;23(11):904–11.
7. Applegate M, Wiggins M, Bailit JL. Are trends in the proportions of non-medically indicated inductions different by Medicaid status?J Perinatol2015;35(5):353–6. [PubMed: 25521560]
8. Grobman W, Rice MM, Reddy UM, et al.Labor induction versus expectant management in low-risk nulliparous women. N Engl J Med2018; 379(6):513–23. [PubMed: 30089070]
9. Main EK, Chang SC, Cheng YW, et al.Hospital-Level variation in the frequency of cesarean delivery among nulliparous women who undergo labor induction. Obstet Gynecol2020;136(6):1179–89. [PubMed: 33156193]
10. ACOG Committee Opinion No 579: Definition of term pregnancy. Obstet Gynecol2013;122(5):1139–40. [PubMed: 24150030]
11. Cunningham FG, Leveno KJ, Bloom SL, et al.Chpt 21: Physiology of Labor. Williams Obstetrics, 25e: McGraw Hill Education; 2018:400–420.
12. Arrowsmith S, Wray S, Quenby S. Maternal obesity and labour complications following induction of labour in prolonged pregnancy. BJOG2011;118(5):578–88. [PubMed: 21265999]
13. Roos N, Sahlin L, Ekman-Ordeberg G, Kieler H, Stephansson O. Maternal risk factors for postterm pregnancy and cesarean delivery following labor induction. Acta Obstet Gynecol Scand2010;89(8):1003–10. [PubMed: 20636240]
14. Morken NH, Melve KK, Skjaerven R. Recurrence of prolonged and post-term gestational age across generations: maternal and paternal contribution. BJOG2011;118(13):1630–5. [PubMed: 21985579]
15. Perinatology Bishop Score Calculator. Available from: http://perinatology.com/calculators/Bishop%20Score%20Calculator.htm [Accessed September 10 2019].
16. California Maternal Quality Care Collaborative. Induction of Labor Algorithm. CMQCC.org. Available from: https://www.cmqcc.org/resource/appendix-r-induction-labor-algorithm Published [4 23, 2019]. Accessed [December 4, 2019].
17. Penfield CA, Wing DA. Labor Induction Techniques: Which Is the Best?Obstetrics and Gynecology Clinics of North America2017;44(4):567–82. [PubMed: 29078939]

18. Hanley GE, Munro S, Greyson D, et al.Diagnosing onset of labor: A systematic review of definitions in the research literature. BMC Pregnancy and Childbirth2016;16(1):71. [PubMed: 27039302]
19. Grobman WA, Bailit J, Lai Y, et al.Defining failed induction of labor. Am J Obstet Gynecol2018;218(1):122 e1–e8. [PubMed: 29138035]
20. American College of Obstetricians and Gynecologists, the Society for Maternal-Fetal Medicine, Caughey AB, Cahill AG, Guise JM, et al.Safe prevention of the primary cesarean delivery. Am J Obstet Gynecol2014;210(3):179–93. [PubMed: 24565430]
21. Freret TS, Woods GT, James KE, Kaimal AJ, Clapp MA. Incidence of and Risk Factors for Failed Induction of Labor Using a Contemporary Definition. Obstet Gynecol2021;137(3):497–504. [PubMed: 33543905]
22. Finucane EM, Murphy DJ, Biesty LM, et al.Membrane sweeping for induction of labour. Cochrane Database Syst Rev2020;2:CD000451. [PubMed: 32103497]
23. Akins ML, Luby-Phelps K, Bank RA, Mahendroo M. Cervical softening during pregnancy: Regulated changes in collagen cross-linking and composition of matricellular proteins in the mouse. Biology of Reproduction2011;84(5):1053–62. [PubMed: 21248285]
24. Kabiri D, Hants Y, Yarkoni TR, Shaulof E, Friedman SE, Paltiel O, et al.Antepartum membrane stripping in GBS carriers, is it safe? (The STRIP-G Study). PloS one2015;10(12):e0145905. [PubMed: 26719985]
25. Prevention of Group B Streptococcal Early-Onset Disease in Newborns: ACOG Committee Opinion, Number 782. Obstet Gynecol2019;134(1):e19–e40.
26. Avdiyovski H, Haith-Cooper M, Scally A. Membrane sweeping at term to promote spontaneous labour and reduce the likelihood of a formal induction of labour for postmaturity: a systematic review and meta-analysis. J Obstet Gynaecol2019;39(1):54–62. [PubMed: 30284490]
27. Liu J, Song G, Meng T, Zhao G. Membrane sweeping added to formal induction method to increase the spontaneous vaginal delivery: a meta-analysis. Arch Gynecol Obstet2018;297(3):623–30. [PubMed: 29288320]
28. Molina PFemale Reproductive System. In: Molina PE, ed. Endocrine Physiology. McGraw-Hill Education; 2018. 217–252.
29. Milton AS. The Role of Prostaglandins in Pyrexia. Biochemical Society Transactions, 575th meeting, Glasgow.
30. Pierce S, Bakker R, Myers DA, Edwards RK. Clinical insights for cervical ripening and labor induction using prostaglandins. AJP Rep2018;8(4):e307–e14. [PubMed: 30377555]
31. U.S. Food and Drug Administration. Misoprostol (marketed as Cytotec) information: Drug safety and availability. n.d. Available from: https://www.fda.gov/Drugs/DrugSafety/ucm111315.htm [Accessed March 21 2018].
32. Benalcazar-Parra C, Monfort-Orti R, Ye-Lin Y, et al.Comparison of labour induction with misoprostol and dinoprostone and characterization of uterine response based on electrohysterogram. J. Matern. -Fetal Neonatal Med2019;32(10):1586–94. [PubMed: 29251182]
33. Haas DM, Daggy J, Flannery KM, et al.A comparison of vaginal versus buccal misoprostol for cervical ripening in women for labor induction at term (the IMPROVE trial): a triple-masked randomized controlled trial. Am J Obstet Gynecol2019;221(3):259 e1–e16. [PubMed: 31075246]
34. Pimentel VM, Arabkhazaeli M, Moon JY, et al.Induction of labor using one dose vs multiple doses of misoprostol: a randomized controlled trial. Am J Obstet Gynecol2018; 218(6):614.e1–614.e8. [PubMed: 29614276]
35. Alfirevic Z, Aflaifel N, Weeks A. Oral misoprostol for induction of labour. Cochrane Database Syst Rev2014(6):CD001338. [PubMed: 24924489]
36. Rouzi AA, Alsahly N, Alamoudi R, et al.Randomized clinical trial between hourly titrated and 2 hourly static oral misoprostol solution for induction of labor. Am J Obstet Gynecol2017;216(4):405 e1–e6. [PubMed: 27986461]
37. Mitchell MD, Flint AP, Bibby J, et al.Rapid increases in plasma prostaglandin concentrations after vaginal examination and amniotomy. BMJ1977;2(6096):1183–5. [PubMed: 589075]
38. Rath W, Kehl S. The renaissance of transcervical balloon catheters for cervical ripening and labour induction. Geburtshilfe Frauenheilkd2015;75(11):1130–9. [PubMed: 26719596]

39. Lajusticia H, Martinez-Dominguez SJ, Perez-Roncero GR, Chedraui P, Perez-Lopez FR. Single versus double-balloon catheters for the induction of labor of singleton pregnancies: a meta-analysis of randomized and quasi-randomized controlled trials. Arch Gynecol Obstet2018;297(5):1089–100. [PubMed: 29445926]
40. Smith H, Peterson N, Lagrew DC, Main E. Toolkit to Support Vaginal Birth and Reduce Primary Cesareans: A Quality Improvement Toolkit. Stanford, CA: California Maternal Quality Care Collaborative (CMQCC); 2016. Available from: https://www.cmqcc.org/VBirthToolkit.Accessed [March 16, 2021].
41. Katz Eriksen JL, Chandrasekaran S, Delaney SS. Is Foley catheter use during a trial of labor after cesarean associated with uterine rupture?Am J Perinatol201912;36(14):1431–1436. [PubMed: 31146296]
42. Vaginal Birth After Cesarean Delivery. ACOG Practice Bulletin No. 205. Obstet Gynecol2019;133(2):e110–e27. [PubMed: 30681543]
43. Diederen M, Gommers J, Wilkinson C, Turnbull D, Mol B. Safety of the balloon catheter for cervical ripening in outpatient care: complications during the period from insertion to expulsion of a balloon catheter in the process of labour induction: a systematic review. BJOG2018;125(9):1086–95. [PubMed: 29211328]
44. Levine LD, Downes KL, Elovitz MA, Parry S, Sammel MD, Srinivas SK. Mechanical and Pharmacologic Methods of Labor Induction: A Randomized Controlled Trial. Obstet Gynecol2016;128(6):1357–64. [PubMed: 27824758]
45. Leopold B, Sciscione A. Is there a place for outpatient preinduction cervical ripening?Obstet Gynecol Clin North Am2017;44(4):583–91. [PubMed: 29078940]
46. Son SL, Benson AE, Hart Hayes E, Subramaniam A, Clark EAS, Einerson BD. Outpatient cervical ripening: A cost-minimization and threshold analysis. Am J Perinatol20202;37(3):245–251. [PubMed: 31430827]
47. Fruhman G, Gavard JA, Amon E, Flick KV, Miller C, Gross GA. Tension compared to no tension on a Foley transcervical catheter for cervical ripening: a randomized controlled trial. Am J Obstet Gynecol2017;216(1):67.e1–.e9. [PubMed: 27640940]
48. Schoen CN, Saccone G, Backley S, et al.Increased single-balloon Foley catheter volume for induction of labor and time to delivery: a systematic review and meta-analysis. Acta Obstet Gynecol Scand2018;97(9):1051–60. [PubMed: 29607491]
49. McMaster K, Sanchez-Ramos L, Kaunitz AM. Evaluation of a transcervical foley catheter as a source of infection: A Systematic Review and Meta-analysis. Obstet Gynecol2015;126(3):539–51. [PubMed: 26244535]
50. Zhu L, Zhang C, Cao F, Liu Q, Gu X, Xu J, et al.Intracervical Foley catheter balloon versus dinoprostone insert for induction cervical ripening: A systematic review and meta-analysis of randomized controlled trials. Medicine2018;97(48):e13251. [PubMed: 30508911]
51. Tuuli MG, Keegan MB, Odibo AO, Roehl K, Macones GA, Cahill AG. Progress of labor in women induced with misoprostol versus the Foley catheter. Am J Obstet Gynecol2013;209(3):237.e1–7. [PubMed: 23659988]
52. Wollmann CL, Ahlberg M, Petersson G, Saltvedt S, Stephansson O. Time-to-delivery and delivery outcomes comparing three methods of labor induction in 7551 nulliparous women: a population-based cohort study. J Perinatol2017;37(11):1197–203. [PubMed: 29138519]
53. Sarreau M, Isly H, Poulain P, Fontaine B, Morel O, Villemonteix P, et al.Balloon catheter vs oxytocin alone for induction of labor in women with a previous cesarean section: A randomized controlled trial. Acta Obstet Gynecol Scand2020;99(2):259–66. [PubMed: 31432510]
54. Prelabor Rupture of Membranes: ACOG Practice Bulletin, Number 217. Obstet Gynecol2020;135(3):e80–e97. [PubMed: 32080050]
55. Alfirevic Z, Kelly AJ, Dowswell T. Intravenous oxytocin alone for cervical ripening and induction of labour. Cochrane Database Syst Rev2009;2009(4):CD003246–CD.
56. Ornat L, Alonso-Ventura V, Bueno-Notivol J, et al.Misoprostol combined with cervical single or double balloon catheters versus misoprostol alone for labor induction of singleton pregnancies: a meta-analysis of randomized trials. J Matern Fetal Neonatal Med2020;33(20):3453–68. [PubMed: 30741051]

57. Bala A, Bagga R, Kalra J, Dutta S. Early versus delayed amniotomy during labor induction with oxytocin in women with Bishop's score of >=6: a randomized trial. J Maternal Fetal Med2018;31(22):2994–3001.
58. Battarbee AN, Glover AV, Stamilio DM. Association between early amniotomy in labour induction and severe maternal and neonatal morbidity. Aust N Z J Obstet Gynaecol2019.
59. De Vivo VCL, Saccone G, et al. . Early amniotomy after cervical ripening for induction of labor: a systematic review and meta-analysis of randomized controlled trials. Am J Obstet Gynecol 2020;222(4):320–9. [PubMed: 31398311]
60. Hawkins JS, Wing DA. Current pharmacotherapy options for labor induction. Expert Opin Pharmacother2012;13(14):2005–14. [PubMed: 22963686]
61. Lavie A, Shinar S, Hiersch L, Ashwal E, Yogev Y, Aviram A. Uterine electrical activity, oxytocin and labor: translating electrical into mechanical. Arch Gynecol Obstet2018;297(6):1405–13. [PubMed: 29453654]
62. Harper LM, Caughey AB, Odibo AO, Roehl KA, Zhao Q, Cahill AG. Normal progress of induced labor. Obstet Gynecol2012;119(6):1113–8. [PubMed: 22569121]
63. Saccone G, Ciardulli A, Baxter JK, et al.Discontinuing oxytocin infusion in the active phase of labor: A Systematic Review and Meta-analysis. Obstet Gynecol2017;130(5):1090–6. [PubMed: 29016497]
64. Boie S, Glavind J, Velu AV, Mol BWJ, Uldbjerg N, de Graaf I, et al.Discontinuation of intravenous oxytocin in the active phase of induced labour. Cochrane Database Syst Rev2018;8:CD012274. [PubMed: 30125998]
65. Fuchs AR, Romero R, Keefe D, Parra M, Oyarzun E, Behnke E. Oxytocin secretion and human parturition: pulse frequency and duration increase during spontaneous labor in women. Am J Obstet Gynecol1991;165(5 Pt 1):1515–23. [PubMed: 1957888]
66. Simpson KR. Clinicians' guide to the use of oxytocin for labor induction and augmentation. J Midwifery Women's Health2011;56(3):214–21. [PubMed: 21535370]
67. Uvnäs-Moberg K, Ekström-Bergström A, Berg M, Buckley S, Pajalic Z, Hadjigeorgiou E, et al.Maternal plasma levels of oxytocin during physiological childbirth – a systematic review with implications for uterine contractions and central actions of oxytocin. BMC Pregnancy and Childbirth2019;19(1):285. [PubMed: 31399062]
68. Clark S, Belfort M, Saade G, et al.Implementation of a conservative checklist-based protocol for oxytocin administration: maternal and newborn outcomes. AJOG2007;197(5):480.e1–.e5.
69. Seitchik J, Amico J, Robinson AG, Castillo M. Oxytocin augmentation of dysfunctional labor: IV. Oxytocin pharmacokinetics. AJOG1984;150(3):225–8.
70. Blanks AM, Thornton S. The role of oxytocin in parturition. BJOG2003;110(s20):46–51.
71. Simpson KR. Cervical Ripening and Labor Induction and Augmentation, 5th Edition. Nurs Womens Health2020;24(4):S1–s41. [PubMed: 32778395]
72. Budden A, Chen LJY, Henry A. High-dose versus low-dose oxytocin infusion regimens for induction of labour at term. Cochrane Database Syst Rev2014(10).
73. Prichard N, Lindquist A, Hiscock R, Ruff S, Tong S, Brownfoot FC. High-dose compared with low-dose oxytocin for induction of labour of nulliparous women at term. J Matern Fetal Neonatal Med2019;32(3):362–8. [PubMed: 28889775]
74. Leduc D, Biringer A, Lee L, Dy J. Induction of labour. JOGC2013;35(9):840–57. [PubMed: 24099451]
75. Daly D, Minnie KCS, Blignaut A, et al.How much synthetic oxytocin is infused during labour? A review and analysis of regimens used in 12 countries. PloS one2020;15(7):e0227941. [PubMed: 32722667]

Quick points:

- To decrease rates of failed labor induction, providers need to utilize current evidence on labor induction.
- Evidence supports use of prostaglandins or cervical balloons to complete cervical ripening (Bishop score greater than or equal to 6 for multiparous people, greater than or equal to 8 for nulliparous people) before initiating synthetic oxytocin or amniotomy.
- Combination methods of cervical ripening, compared to single method options, safely shorten labor duration for nulliparous people.
- Synthetic oxytocin is best reserved for contraction stimulation after completion of cervical ripening and may be discontinued during the active phase of induced labor in most people.

Table 1.

The Bishop Score

Score	Dilation (cm)	Position of Cervix	Cervical Consistency	Effacement (%)	Station (−3 to +3)
0	Closed	Posterior	Firm	0–30	−3
1	1–2	Mid-position	Medium	40–50	−2
2	3–4	Anterior	Soft	60–70	−1, 0
3	5–6	Anterior	Soft	80 or higher	+1, +2

Adapted from the Perinatology Bishop Score Calculator.[15]

Table 2.

Cervical Ripening Methods for Term Labor Induction

Cervical Ripening Method Generic (Brand)	Routes	Dose Options	Tips for Optimal Use from State of the Science Review of Literature
PGE_1 analogue: Misoprostol (Cytotec)	Vaginal, buccal, oral	25–50 mcg every 4–6 h	-Associated with shorter labor durations without increasing uterine hyperstimulation or meconium-stained amniotic fluid in nulliparous persons when compared to dinoprostone.[32] -Single-dosing regimen prior to oxytocin initiation only acceptable for those with Bishop score > 4 after first dose, or multiparous people.[34] -In nulliparous people, vaginal dosing should be repeated up to 7 doses until cervical ripening is complete (Bishop score at least 8).[34] -If available, oral solution (25 mcg every 2 h) is superior to dinoprostone or oxytocin for lowering risk of cesarean birth without increasing incidence of uterine hyperstimulation.[35] -Buccal administration is inferior to vaginal administration for labor duration, cesarean birth, and non-reassuring fetal status in people with intact membranes.[33] -Not appropriate for persons with prior uterine surgery.
PGE_2 analogue: Dinoprostone (Cervidil, Prepidil)	Vaginal insert (10mg) Cervical gel (0.3 mg/h)	Vaginal insert: 12 h Cervical gel: every 6h	-Vaginal insert form of dinoprostone may be preferred over vaginal misoprostol tablets or oral dosing in settings where there are concerns for fetal tolerance of contractions (cervical balloons also options in these cases). -Not appropriate for persons with prior uterine surgery.
Cervical balloons	Intracervical	Fill 30–90mL	-Localized action with few systemic side effects and easy discontinuation make cervical balloons optimal, especially for outpatient cervical ripening or people desiring VBAC.[41, 43–45] -No difference between single-balloon (Foley catheter) and double-balloon (Cook's catheter) device on effectiveness or major maternal/neonatal outcomes.[39] -No difference on time to birth for balloons placed with vs. without tension.[47] -Higher balloon fill compared to lower fill volumes (60mL compared to 30mL) shortens IOL duration.[48] -If membranes are intact, balloons do not increase risk of infection compared to vaginally-administered prostaglandins.[49, 50] -Cervical ripening with cervical balloons differs from misoprostol whereby early labor progression (1cm-4cm) is quicker, but later labor (4cm-10cm) proceeds slower with no overall difference.[51] -In nulliparous people, balloon with moderate fill (50mL) shortens labor compared to misoprostol and the dinoprostone vaginal insert.[52]
Oxytocin	Intravenous	Varies	Not recommended as a solo agent for cervical ripening unless in cases of prior cesarean birth or other contraindications of prostaglandins or cervical balloons. Use for contraction stimulation should be delayed until Bishop scores reach at least 6 for people who are multiparous or 8 for nulliparous.[16]

Cervical Ripening Method Generic (Brand)	Routes	Dose Options	Tips for Optimal Use from State of the Science Review of Literature
Combination Methods (misoprostol + cervical balloon or oxytocin + cervical balloon)	Vaginal or oral (misoprostol) Or intravenous (oxytocin) + intracervical (balloon)	25mcg (misoprostol) Varies (oxytocin) 30–50mL fill (balloon)	*Compared to misoprostol as a single agent:* -combination treatment with misoprostol + cervical balloon shorted duration of induction-to-birth.[44, 56] -combination of misoprostol + cervical balloon also may decrease rates of uterine hyperstimulation and NICU admission. -combination of oxytocin + balloon shortens median time to birth.[56] *Compared to cervical balloon as a single agent:* -nulliparous people with combination of balloon + oxytocin were more likely to finish IOL with vaginal birth within 24 hours.[50] -no difference in multiparous people for solo balloon vs. combo with oxytocin.[50]

Abbreviations: NICU, neonatal intensive care unit; cm, centimeters; mL, milliliters; VBAC, vaginal birth after cesarean; mcg, micrograms; h, hours

Table 3.

Clinical Guidance for Use of Exogenous Oxytocin (Pitocin)

Organizational Dosing Recommendations				Adverse Side Effects	Tips for Optimal Use from State of the Science Review of Literature
	AWHONN [71]	**ACOG** [2] **Low-dose regimen**	**SOGC Low-dose regimen** [74]	Uterine tachysystole, Fetal heart rate changes, Meconium staining of amniotic fluid, Placental abruption, Amniotic fluid embolism, and Water intoxication[75]	For cervical ripening: Initiate with Bishop score <4 only if contraindications to prostaglandins.[34]
Starting dose	1 mU/min	0.5–2 mU/min	1–2 mU/min		
Increment dose	1–2 mU/min	1–2 mU/min	1–2 mU/min		*For latent phase of induction of labor:* Latent labor occurs over a longer duration than spontaneous labor (hours to move from 3–6cm dilation: nulliparous 19.2h IOL vs. 7h SOL; multiparous 22.3h IOL vs 5.9h SOL).[62]
Frequency of dose increase	Every 30–60 minutes	Every 15–40 minutes	Every 30 minutes		*For active phase of induction of labor:* Consider reducing the infusion rate or discontinuing oxytocin infusion.[63]
Maximum dose	20 mU/min	None	30 mU/min (Denotes “usual dose” for labor 8–12 mU/min)		An infusion rate of 11–13 mU/min has been identified as the rate where most women should experience adequate contractions and cervical change.[68]

Abbreviations: ACOG, American College of Obstetricians and Gynecologists; AWHONN, Association of Women’s Health, Obstetric and Neonatal Nurses; SOGC, The Society of Obstetricians and Gynaecologists of Canada; IOL, induction of labor; SOL, spontaneous onset of labor; mU, milliunits; min, minutes.