

Induction of Labor

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INTRODUCTION

The need for artificially stimulating the process of delivery has been known since long and the indications have only grown over the last century. Initially, it was done to expel a dead fetus, then came the realization that in certain conditions, like hypertensive disorders of pregnancy, induction of labor could be beneficial to both, the mother as well as the baby. The early methods of inducing labor involved mechanical manipulations, including douches, tents, bougies and catheters. Then came the administration of potions and latterly castor oil, quinine and posterior pituitary extract. A number of amusing folkloric or old midwives' approaches are still used today by women to encourage their labor to start. Among them the more common are frequent walking, vaginal intercourse, participating in heavy exercise, consumption of laxatives, spicy foods or herbal tea, nipple stimulation and administration of an enema.¹ Other methods, like consumption of Chinese food/warm gin/cranberry juice, are also believed to be helpful in initiating labor. Discovery of pharmacological myometrial stimulants and their use along with the mechanical methods characterized the latter half of the twentieth century. In the last two decades, patients' expectations of when and how delivery will be achieved have become a significant and sometimes overpowering consideration. The rates of labor induction have risen to reach 20% of all labors in developed countries. The WHO Global Survey on maternal and perinatal health (including data from 24 countries and nearly 300,000 deliveries) showed that 9.6% of the deliveries involved labor induction. Overall, the survey found that facilities in African countries tended to have lower rates of induction of labor (lowest: Niger 1.4%) compared with Asian and Latin American countries (highest: Sri Lanka 35.5%).²

Definitions

Induction of labor is the stimulation of uterine contractions using medical or surgical means prior to spontaneous labor in order

to achieve a vaginal birth. Augmentation on the other hand, means stimulating more uterine contractions when the process of labor has already started (if the contractions are inadequate progress of labor is slow). Cervical ripening is a preparatory process occurring prior to labor in which the cervix progressively softens, thins out and dilates.

INDICATIONS

Generally, induction of labor is indicated when the benefits of early delivery are greater than the risks of continuing the pregnancy. Labor induction, however, is not without its own problems and must be weighed against the potential maternal and fetal risks associated with this procedure. Indications for induction of labor are not absolute but should take into account maternal and fetal conditions, gestational age, cervical status and other factors. A list of indications for induction is enumerated in Table 1.

Hypertensive Disorders of Pregnancy

Delivery is the only definitive treatment with PIH. In preterm pregnancies (below 34 weeks) complicated by preeclampsia, conservative management (corticosteroids, antihypertensives, seizure prophylaxis with MgSO₄, with close monitoring) is advocated to increase the chance of fetal maturity as long as the risks for the mother remain acceptable. Induction of labor in PIH can be done for fetal indications, like severe intrauterine growth restriction, nonreassuring fetal surveillance and oligohydramnios, or for maternal indications, like progressive deterioration of hepatic/renal function, HELLP syndrome, symptoms of imminent eclampsia, suspected placental abruption, progression to eclampsia or if the woman has reached a gestational age of 38 weeks or greater. It is common to induce labor in women after 37 to 38 weeks even with mild PIH/PET given its unpredictable complications, like placental abruption.

Table 1: Indications and contraindications for induction of labor

<i>Indications</i>	<i>Contraindications</i>
Hypertensive disorders of pregnancy	Vasa previa or complete placenta previa
Postdated pregnancy	Transverse fetal lie
Premature rupture of membranes	Umbilical cord prolapse
Intra-amniotic infection (chorioamnionitis)	Previous classical cesarean delivery
Intrauterine growth restriction	Active genital herpes infection
Fetal complications (isoimmunization, oligohydramnios, nonreassuring fetal status)	Previous myomectomy entering the endometrial cavity
Maternal medical complications (APLA/DM/renal disease/SLE)	Contracted pelvis, severe degree of cephalopelvic disproportion
Intrauterine fetal death	Previous rupture uterus

Induction of labor might prevent maternal and neonatal complications at the expense of increased instrumental vaginal delivery and CS rates.

Postdated Pregnancy

This is presently the commonest indication for labor induction, as prolonged pregnancy is associated with increased morbidity due to macrosomia, birth trauma, meconium aspiration and placental insufficiency which increase with advancing gestation. The policy of offering routine induction of labor after 41 weeks does not increase the chances of delivery by CS and might even lead to a reduction in the CS risk.³

PROM/pPROM

If a woman has preterm prelabor rupture of membranes (pPROM), induction of labor should not be carried out before 34 weeks unless there are additional obstetric indications (for example, infection or fetal compromise). Prelabor rupture of membranes (PROM) occurs in 6 to 19% of term pregnancies and most women will go into labor within 24 hours of rupture of membranes. The risks of maternal and fetal infection increase as time between the rupture of membranes and the onset of labor increases. Comparison of expectant management versus induction showed no change in the operative delivery or CS rate, but showed a reduction in the infective sequelae in both mother and baby. Thus, it is now recommended that women should be offered induction at no later than 24 hours post-PROM.⁴

Intrauterine Fetal Demise

Induction of labor is a viable option to expectant management. Majority of the women will have a spontaneous onset labor within the next three weeks. Expectant management gives the mother adequate time to come in terms with the adverse outcome. Induction should not be based on the theoretical risk of disseminated intravascular coagulation (DIC), unless the fetal death is a result of placental abruption or PIH. DIC associated with intrauterine fetal demise (IUID) usually develops late (up to 25% risk 4 weeks after the fetal death).

Maternal Diabetes Mellitus

Diabetic pregnancies are complicated by fetal macrosomia, increased chances of cesarean section, instrumental delivery, shoulder dystocia and unexplained stillbirths. Pregnant women

with diabetes who have a normally grown fetus should be offered elective birth through induction of labor, or by elective cesarean section if indicated, after 38 completed weeks.⁵ Pregnant women with diabetes who have an ultrasound-diagnosed macrosomic fetus should be informed of the risks and benefits of vaginal birth, induction of labor and cesarean section.

Fetal Growth Restriction

These babies are compromised and at a high risk of intrauterine hypoxia, perinatal mortality and morbidity. If delivery is necessary due to abnormalities of fetal Doppler [absent/ reversed end-diastolic flow in the umbilical arteries (AEDF/ REDF) or abnormal ductus venosus waveform], induction is unlikely to be successful, as the fetal reserve will be insufficient to tolerate the rigors of an induced labor. Evaluating the favorability of the cervix is important in deciding the route of delivery. If induction is chosen, continuous electronic fetal monitoring is mandatory throughout labor.

CONTRAINDICATIONS

The contraindications to labor induction are generally those conditions where vaginal delivery is not possible (e.g. contracted pelvis) or is associated with increased morbidity (e.g. active genital herpes). A list of contraindications is provided in Table 1. Other clinical situations that are not generally considered contraindications to labor induction but warrant caution include breech presentation, borderline clinical pelvimetry, grand multiparity, free floating head, polyhydramnios and multifetal gestation.

Predictors of Successful Induction

Bishop's Score

In 1964, Bishop⁶ developed a scoring system for cervical assessment (Table 2). The Bishop's score helps to delineate the patients who would be most likely to achieve a successful induction. Unfavorable (< 5) Bishop's scores at admission for induction of labor are associated with a two- to threefold increased risk of cesarean delivery when compared with spontaneous onset of labor.^{7,8} A Bishop's score of ≥9 is usually associated with a probability of vaginal delivery after labor induction similar to that after spontaneous labor.⁹ Bishop's scores of less than 6 usually require a preinduction cervical ripening.¹⁰

Table 2: Bishop's score and modified Bishop's (Calder) score

	Score	0	1	2	3
Bishop's score	Cervical dilatation (cm)	Closed	1-2	3-4	5 or >
	Effacement (%)	0-30	40-50	60-70	80 or >
	Station of head	-3	-2	-1.0	+1, +2
	Consistency	Firm	Medium	Soft	—
	Position	Posterior	Midposterior	Anterior	—
Calder's score	Cervical dilatation (cm)	<1	1-2	2-4	>4
	Effacement (cm)	>4	2-4	1-2	<1
	Station of head	-3	-2	-1, 0	+1, +2
	Consistency	Firm	Average	Soft	—
	Position	Posterior	Midanterior	—	—

Fetal Fibronectin

Fetal fibronectin (fFN) concentrations in cervical secretions, which were used for the prediction of preterm labor, have also been shown to correlate with induced labor outcomes. fFN appears to predict the patients who will have shorter and easier inductions of labor and lower cesarean section rates, including nulliparous women with low Bishop's scores.¹¹ A review of eight reports concluded that a positive fFN was associated with significantly shorter delivery intervals than when a negative fFN result is obtained.¹² A positive fFN can aid management by predicting the onset of spontaneous labor within days, so that the patient can be counseled to wait. On the contrary, a negative fFN with a poor bishop's score can defer an induction in the absence of an emergent indication.

Transvaginal Ultrasonography (TVUS)

A short cervical length (CL) (< 20 mm or < 25 mm) on transvaginal ultrasound (TVU) is associated with a short duration of labor and a higher incidence of vaginal delivery compared with longer cervix in women at term undergoing induction.^{13,14} Transvaginal measurement of cervical length measurement is better tolerated than digital examination for Bishop's score assessment.¹⁵

Recent comparison of clinical history, digital examination, cervical ultrasound and fetal fibronectin assay in predicting successful labor induction at term found that only history and digital examination predicted vaginal delivery within 24 hours accurately and were independently associated with labor duration.¹⁶ Fetal fibronectin and ultrasound measurements failed to predict accurately the outcome of induced labor.

Others

These have been used in studies and are not very clinically useful at this point of time. Electrical impedance measurements across the surface of the cervix using an 8 mm tetrapolar pencil probe have been used¹⁷ and a statistically significant association was found with the resistivity and the favorability of the cervix.

Serum nitrite/nitrate levels have also been assayed in nullipara undergoing prostaglandin induction of labor and significantly lower levels of each were found in women who delivered within 15 hours of labor induction compared with those delivering over a longer period.¹⁸

Interventions for Decreasing the Need for Induction

Ultrasonography

Pregnancy dating based on the last menstrual period is subject to inaccuracy due to incorrect recall, delayed ovulation and irregular menses. Compared with no routine early ultrasound, routine early pregnancy (< 20 weeks) ultrasound reduces by 32 to 39% the incidence of post-term pregnancy and of induction for post-term pregnancy.¹⁹

Sweeping of Membranes

Although traditionally considered a method of labor induction, sweeping might not be useful in emergent situations because of

unpredictable response. It acts by causing significant increases in phospholipase A2 activity and prostaglandin F2 α (PGF2 α) levels.²⁰ It is associated with a shorter time between treatment and spontaneous labor, a reduction in the incidence of prolonged pregnancy and the need for the use of formal induction.²¹ Chances of entering spontaneous labor after one sweeping at term are about doubled to 36% in the next 48 hours versus 17% without sweeping. This has to be weighed against the discomfort to the woman, bleeding and irregular contractions. Complications, such as infection and ruptured membranes, are not found to be increased with stripping.²¹

Sexual Intercourse

Semen is presumed to contain the highest prostaglandin concentration of any body fluid. Apart from the direct action of these prostaglandins, other mechanisms that can incite labor include physical stimulation of the lower uterine segment, or endogenous release of oxytocin as a result of orgasm or the Ferguson reflex. It is difficult to standardize sexual intercourse as an intervention disallowing meaningful comparisons with other methods.²²

Nipple stimulation

Breast stimulation has been suggested as an effective inexpensive nonmedical means of inducing labor. In women with a favorable cervix, the Cochrane database review found that a significantly more number of women were in labor 72 hours following the start of nipple stimulation compared with no intervention. Nipple stimulation was also associated with decreased incidence of postpartum hemorrhage. There was, however, no reduction in the need for delivery by cesarean section.²³ Other methods, like acupuncture and homeopathy, have been used variably for initiating labor. However, there is very limited information upon their clinical effectiveness and fetal side effect profile for this purpose.

METHODS FOR RIPENING

Cervical ripening is a complex process that results in physical softening and distensibility of the cervix, ultimately leading to partial cervical effacement and dilatation. Remodeling of the cervix²⁴ involves enzymatic dissolution of collagen fibrils, increase in water content and chemical changes. These changes are induced by hormones (estrogen, progesterone, relaxin) as well as cytokines, prostaglandin and nitric oxide synthesis enzymes. Actually, methods that are used for cervical ripening also cause uterine muscle contraction to some degree and there is no strict demarcation between a ripening and an inducing agent. It is important to understand that the principal role of ripening agents is to soften the unfavorable cervix independently of uterine activity.

Mechanical

Mechanical methods include hygroscopic dilators (laminaria or dilapan), balloon (e.g. Foley), and balloon with extra-amniotic saline infusion (EASI). The techniques for the use of mechanical methods are described in Table 3.

Table 3: Techniques for the use of mechanical methods of ripening

Methods used	Techniques
Hygroscopic dilators	The perineum and vagina are prepped with antiseptic. Using a sterile speculum examination to visualize the cervix, the dilator is introduced into the endocervix, allowing their tails to fall into the vagina. Dilators are progressively placed until the endocervix is full. The number of dilators used is noted in the medical record. A sterile gauze pad is placed in the vagina to maintain the position of the dilators.
Extra-amniotic balloon	The catheter is introduced into the endocervix by direct visualization into the potential space between the amniotic membrane and the lower uterine segment. The balloon reservoir is inflated with 30 to 50 ml of normal saline and it is strapped to the thigh to maintain traction on the internal os
Extra-amniotic saline infusion	Inflate catheter with 40 ml of sterile water or saline. Infuse sterile saline at a rate of 40 ml per hour into the extra-amniotic space using an infusion pump. Remove 6 hours later or at the time of spontaneous expulsion or rupture of membranes (whichever occurs first)

1. *Hygroscopic dilators*: Before the advent of prostaglandin analogs, use of hygroscopic dilators was a popular mechanical method for cervical ripening. Cervical dilators are made from organic seaweed (laminaria) or synthetic hydrophilic materials (lamicel-polyvinyl alcohol polymer–magnesium sulfate and dilapam-polyacrylonitrile). They are introduced into the cervical canal and left *in situ* for 6 to 12 hours, where they increase in diameter because of their hydrophilic properties, achieving a gradual stretching, dilatation and effacement of the cervix. Several studies have shown that these osmotic dilators can also be successfully employed for cervical ripening in viable pregnancies with an unripe cervix.^{25,26} Advantages to the use of osmotic dilators are their low cost and ease of placement and removal, decreased risk of uterine hyperstimulation and that it does not require stringent monitoring of the fetal heart rate. They are contraindicated in cases of ruptured membranes. Their use may cause an increased risk of maternal endometritis and neonatal sepsis due to inability to ensure sterility in the organic product.²⁷
2. *Extra-amniotic balloon*: Foleys's catheter—the Foley catheter affects cervical ripening in two ways: Gradual mechanical dilation and separation of the decidua from the amnion, stimulating prostaglandin release. Many studies have demonstrated the Foley catheter to be an effective tool for achieving a favorable cervix.^{28,29} Its advantages include low cost, safe, well tolerated, can be added to vaginal prostaglandins to decrease the induction delivery interval, decreased incidence of fetal distress and uterine hyperstimulation and possible use even on an outpatient basis,²⁹ saving further costs. It is contraindicated in cases with cervical infection, low-lying placenta, or third trimester bleeding. Foley catheter use is associated with certain complications: Bleeding, fever, displacement of the presenting part and premature rupture of membranes (PROM).
3. *Extra-amniotic saline infusion (EASI)*: Compared to tents and prostaglandins, EASI is associated with shorter intervals to yield a favorable Bishop's score,^{29,30} less nonreassuring fetal heart testing³¹ and similar to lower incidence of cesarean delivery.³²

Medical

1. *Prostaglandins*: Prostaglandins act on the cervix to enable ripening by a number of different mechanisms. They alter the

extracellular ground substance of the cervix, and PGE2 increases the activity of collagenase in the cervix. They cause an increase in gap junctions, elastase, glycosaminoglycan, dermatan sulfate, and hyaluronic acid levels in the cervix. A relaxation of cervical smooth muscle facilitates dilation. Finally, prostaglandins allow for an increase in intracellular calcium levels, causing contraction of myometrial muscle.^{33,34} Two PGE2 preparations are commercially available: 0.5 mg of dinoprostone gel for intracervical application in a 2.5 ml syringe (Prepidil/Cerviprime) and a vaginal insert containing 10 mg of dinoprostone (cervidil). Compared with placebo or oxytocin alone, vaginal prostaglandins used for cervical ripening increase the likelihood of delivery within 24 hours, do not reduce the rate of cesarean delivery, and increase the risk of uterine tachysystole with associated FHR changes.³⁵

For using Prepidil/Cerviprime,³⁶ bring gel to room temperature before application. Introduce the gel into the endocervix just below the level of the internal os under vision. After application of the gel, the patient should remain recumbent for 30 minutes before being allowed to ambulate. End points for ripening include strong uterine contractions, a Bishop's score of ≥ 8 , or a change in maternal or fetal status. Maximum recommended dosage is 1.5 mg (3 doses) of dinoprostone in 24 hours. Do not start oxytocin for 6 to 12 hours after placement of the last dose, to allow for spontaneous onset of labor and protect the uterus from overstimulation.

For the Cervidil vaginal insert,³⁶ a small amount of water-miscible lubricant is used and the tab placed into the posterior fornix of the cervix. As the device absorbs moisture and swells, it releases dinoprostone at a rate of 0.3 mg per hour for 12 hours. After insertion, the patient should remain recumbent for 2 hours. Remove the insert by pulling the cord after 12 hours, when active labor begins, or if uterine hyperstimulation occurs. The advantage of PGE2 analogs is that they are associated with higher delivery rates compared to oxytocin alone, even in women with an unfavorable Bishop's score. However, the advantage is offset by the high cost, need for refrigeration and the risk for uterine hypertonus/tachysystole.

2. *Mifepristone*: Mifepristone is an antiprogesterin agent that causes decrease in cervical tensile strength, decrease in collagen organization and collagen fragmentation with a significant decrease in fibril length and diameter. Matrix metalloproteinase-2 expression is also increased after the administration of mifepristone.³⁷ Compared with placebo, mifepristone is associated with a lower incidence of an unfavorable cervix at

Table 4: Comparison of the available prostaglandin analogs

Attributes	Intracervical PGE2 gel <i>Prepidil/Cerviprime</i>	Vaginal PGE2 insert <i>Cervidil</i>	PGE1 analog <i>Misoprostol</i>
Availability	Sterile viscous gel in syringe— 0.5 mg PGE2 per 3.0 gm	Thin flat polymeric slab of 10 mg PGE2 pessary in a knitted polyester system.	25, 100 and 200 mcg tablets. Vaginal route preferable
Pharmacokinetics	T1/2 < 5 mins	T1/2 = 2.5-5 mins, sustained release of ~0.3 mg/hr <i>in vivo</i>	T1/2 = 20-40 mins
Initial dose	0.5 mg	10 mg	25-50 mcg
Maximum dose	3 doses/24 hrs	1 dose	6 doses/24 hrs
Refrigeration	Required	Required	Not required
Oxytocin administration	6-12 hrs after the last dose	30-60 mins after removal of the insert	Minimum 3 hrs after last dose of PGE1
Lying down period after application	30 mins	2 hrs	30 mins

48 or 96 hours, higher incidence of delivery within 48 and 96 hours, and lower incidence of cesarean section.³⁸ There is insufficient evidence to support a particular dose but a single dose of 200 mg mifepristone appears to be the lowest effective dose for cervical ripening.³⁸ Abnormal fetal heart rate patterns were more common after mifepristone treatment but there was no evidence of differences in other neonatal outcomes.³⁸ Questions remain over its effect on fetal/neonatal adrenal function.

Several other approaches to cervical ripening have been documented in literature. Some of them include use of estrogens (intramuscular, endocervical, vaginal and extra-amniotic), intravenous dehydroepiandrosterone sulphate (DHEAS), hyaluronidase intracervical injections, relaxin gel, oral nitric oxide donors, etc. None of them were found to be clinically useful and they have now been superseded by the use of mechanical methods and prostaglandins.

METHODS FOR INDUCTION

Surgical

Artificial rupture of membranes (ARM)/Amniotomy: Amniotomy is a simple procedure, which can be used alone for induction of labor if the membranes are accessible, sometimes avoiding the need for pharmacological intervention. Amniotomy causes release of endogenous prostaglandins that can initiate labor. However, if performed in a woman with an unfavorable cervix, amniotomy may be followed by long and unpredictable intervals before onset of labor. Although early amniotomy may be associated with shorter labor, it is also associated with an increase in nonreassuring fetal heart rate patterns consistent with cord compression and chorioamnionitis.³⁹ Risks associated with this procedure include umbilical cord prolapse or compression, maternal or neonatal infection, FHR deceleration, bleeding from placenta previa or low-lying placenta and possible fetal injury. Contraindications to ARM include maternal HIV, mother positive for group B streptococcus, where the chances of transmitting the infection to the baby are increased with increasing duration of rupture of membranes. Other contraindications include a free floating head, ill applied cervix and vasa previa. There are clinical situations where amniotomy alone may be considered, such as in grand multiparous women and women with previous CS, where the risk of scar rupture with prostaglandins and oxytocin are higher than if labour starts spontaneously. Currently, amniotomy is recommended 6 hours

after the last use of prostaglandin for induction and oxytocin is either started immediately or within a short interval of 2 to 4 hours.

Medical

1. *Misoprostol:* Misoprostol is a synthetic PGE1 analog, used as an antigastric ulcer agent and used off-label in obstetric practice for first/second trimester medical termination of pregnancy (MTP) and for ripening of cervix. However, as majority of patients experience regular uterine contractions soon after the initial dose, misoprostol should be considered primarily a labor induction agent, which occasionally ripens the cervix without uterine activity. Mechanism of action—PGE1 stimulates uterine contractions and cervical dilation by potentiating calcium ion transport across the cellular membrane and regulation of cyclic adenosine monophosphate (cAMP) within the uterine smooth muscle cells. Additionally, PGE1 stimulates the pathway leading to the activation of collagenases which, in turn, break down the structural collagen network of the cervix, yielding a softer, thinner cervix. Its advantages include stability at room temperature and effectiveness even if taken orally. It is also considerably cheaper than the alternative PGE2 analogs. Use of misoprostol is associated with an overall lower incidence of cesarean section, a higher incidence of vaginal delivery within 24 hours of application and a reduced need for oxytocin augmentation.⁴⁰ Disadvantages of misoprostol include a higher incidence of side effects, like cramps, shivering, fever, which are usually self-limited. More serious side effects include uterine hyperstimulation, meconium staining of the amniotic fluid and risk of uterine rupture, especially in women with previously scarred uteri. Side effects are dose dependant with higher doses or shorter dosing intervals are associated with greater risk of hyperstimulation.

Dosage: It has been used vaginally, orally and sublingually. Vaginal misoprostol appears to be more effective than the equivalent dosage administered orally, but is associated with a higher risk of uterine hyperstimulation both with and without FHR changes. Raising the dose given orally to increase effectiveness causes the same side effects. Although found useful in some trials, there is yet inadequate data to recommend sublingual or buccal use of misoprostol. It appears that the optimal dose and dosing interval is 25 mcg intravaginally every 4 to 6 hours.⁴¹

2. *Oxytocin:* It is a synthetic polypeptide and is the preferred pharmacologic agent for inducing labor when the cervix is

favorable or ripe. As pregnancy progresses, the number of oxytocin receptors in the uterus increases (by 100-fold at 32 weeks and by up to 300-fold at the onset of labor). Oxytocin activates the phospholipase C-inositol pathway and increases intracellular calcium levels, stimulating contractions in myometrial smooth muscle.³⁴ Advantages of oxytocin include a short plasma half life (3-6 mins), ability to titrate the dose with uterine activity and even stopping the drip if required. Disadvantages include need for a running IV drip, which restricts ambulation, loss of potency with exposure to heat/ light and its propensity to retain water, hypotension (especially with inadvertent IV bolus), hyponatremia due to antidiuretic properties (especially when dilute solutions given in high volumes) and increased risk of neonatal hyperbilirubinemia.

Dosage: Numerous intravenous oxytocin regimens have been studied and the optimal protocol remains uncertain. The low-dose regimens are safer and attempt to mimic the physiologic release of oxytocin, commonly beginning with a 1 mU per minute initial dose, increased by 1 to 2 mU per minute at 40 to 60 minutes intervals. High-dose regimens begin with an initial dose of 6 mU per minutes, increased by 6 mU per minute every 15 to 30 minutes. Labor and delivery protocols typically include a maximum infusion rate of 40 mU per minute. However, it is important to note that only less 10% of women will require more than 16 mU/min to establish satisfactory uterine activity. Higher infusion rates may be occasionally used only after consultation with a senior obstetrician. The high-dose protocol, while associated with a more rapid initiation of induction to delivery time, was also found to have a higher rate of hyperstimulation. Cesarean delivery rates did not differ between the various protocols.⁴² However, the need for strict monitoring and adequate round the clock medical staff for supervision of the parturient is of utmost importance with high dose regimens. The typical protocol used in our unit, which can be used in the absence of infusion, the pump is described in Table 5.

Table 5: Preparing an oxytocin drip

Add 1 unit of oxytocin to 500 ml of normal saline. Therefore, it is equal to 1000 mU/500 ml or 2 mU/ml of the NS drip. As 1 ml equals 16 drops, 2 mU/ml = 2 mU/16 drops or 1 mU/8 drops. If fluid restriction is indicated as in case of severe pre-eclampsia or severe anemia, prepare a concentrated drip with 10 units in 500 ml NS and adjust drip rate accordingly. Doses are increased every 20 to 40 mins by either increasing drip rate or adding additional units of oxytocin			
	<i>Units of oxytocin in 500 ml NS</i>	<i>Drip rate (drops/min)</i>	<i>Dose of oxytocin (mU/min)</i>
High dose protocol	1	48	6
	2	48	12
	3	48	18
	4	48	24
	5	48	30
	6	48	36
Low dose protocol	1	8	1
		16	2
		32	4
	2	32	8
	3	32	12
	4	32	16
	5	32	20
	6	32	24

Complications associated with IOL

1. **Tachysystole/Hypertonus/Hyperstimulation:** There has been a great disparity in the definitions of these terms used in studies, making comparisons between drugs difficult. Yet, what we do know is that prostaglandins are associated with significantly increased risk of hypertonus with or without abnormal FHR tracings. Terms to describe increased uterine activity are now defined by the American College of Obstetricians and Gynecologists (ACOG) as follows: Uterine tachysystole is defined as ≥ 6 contractions in a 10-minute period. Uterine hypertonus is described as a single contraction lasting longer than 2 minutes. Uterine hyperstimulation is when either condition leads to a nonreassuring fetal heart rate pattern. Uterine tachysystole typically begins within 1 hour after the gel or insert and peaks at 4 hours after prostaglandin administration. However, it may occur even up to 9 1/2 hours after the vaginal insert has been placed,^{43,44} thus necessitating continuous monitoring of the induced woman. The risk of hyperstimulation with different settings and its management is depicted in Table 6.⁴⁵
2. **Rupture uterus:** The rupture uterus is much more common with induction of labor. Mismanagement of labor with unsupervised use of inducing agents is one of the causes. Table 7 shows the rates of uterine rupture in different scenarios and ripening/ inducing agents.⁴⁶ The ACOG states that the use of misoprostol in women with prior cesarean delivery or major uterine surgery has been associated with an increase in uterine rupture and, therefore, should be avoided in the third trimester.
3. **Failed induction:** Even today, there is no consensus as to what constitutes a failed induction and different studies have used different criteria. Almost 40% of the women who remained in the latent phase after 12 hours of oxytocin and

Table 6: Uterine tachysystole and hyperstimulation in different settings⁴⁵

<i>Setting</i>	<i>Tachysystole (%)</i>	<i>Hyperstimulation (%)</i>
Spontaneous onset of labor (overall)	23.3	2.3
No augmentation	20.9	0.0
Augmentation (oxytocin)	25.6	4.7
Induction with oxytocin	30.2	1.9
Misoprostol vaginal tablet (50 mcg)	48.6	7.6
Misoprostol oral tablet (50 mcg)	22.2	1.9
Dinoprostone intravaginal gel (1 or 2 mg) or intracervical gel (0.5 mg)	33.0	16.5

Intrauterine resuscitation: Remove the tab/vaginal insert or stop the oxytocin drip. Give the mother a left lateral recumbent position to increase the uterine blood flow. To maintain fetal oxygenation, the mother should be given oxygen by face mask at 8-10 l/min. Tocolysis with 0.25 mg of subcutaneous terbutaline should be given if contractions persist. If despite these measures, the nonreactive fetal status continues, prepare for an emergency cesarean delivery. If induction is to be continued, the oxytocin is restarted at half the dose at which hyperstimulation occurred, and the incremental dose rate is also halved.

Table 7: Uterine rupture in different scenarios⁴⁶

Scenarios	Rate of rupture (%)	
Unscarred Uterus	Developed countries	0.012
	Developing countries	0.11
Previous cesarean	Repeat cesarean, no TOL	0.16
	Spontaneous labor	0.44
	Induced TOL oxytocin	0.8
	Induced TOL prostaglandins	1.6
	Induced TOL, combined oxytocin + PG	1.7

membrane rupture were delivered vaginally. Therefore, it is reasonable to avoid deeming labor induction a failure in the latent phase until oxytocin has been administered for at least 12 hours after membrane rupture.⁴⁷ The final decision will depend upon the urgency with which delivery is needed, condition of the mother and baby and the wishes of the woman and her partner. Failed induction is not necessarily an indication for cesarean section. Other options include waiting for spontaneous labor, further use of prostaglandins, reinduction after a period of rest or use of epidural analgesia to allow a difficult ARM.

4. *Cesarean section:* Increasing incidence of labor induction has contributed to the increasing cesarean section rate. Compared to spontaneous onset of delivery, induction of labor is associated with an increased risk for emergency cesarean section both among nulliparous (odds ratio, 3.34) and multiparous women (odds ratio, 1.94).⁴⁸ Other risk factors include nulliparity, poor Bishop's score and elective induction (induction in the absence of any medical/obstetric indication, only done for convenience) prior to term.
5. *Greater need for pain relief:* It is important to discuss pain relief with women who are undergoing induction of labor. Induced labor significantly differs from the physiological spontaneous onset labor, with a longer and often painful latent phase. Prostaglandins may be associated with significant discomfort before the onset of proper labor (so-called 'prostin' pains). Simple analgesia may suffice, but some women will require stronger opiate/epidural analgesia.

KEYPOINTS

- Labor induction is indicated when the benefits of delivery to the mother and/or fetus outweigh the risks of continuing the pregnancy
- More than 80% of inductions are for postdates and hypertension. The indication for the induction and informed consent should always be recorded after explaining its pros and cons
- Ultrasonography prior to 20 weeks and stripping the membranes are associated with a significant decrease in the need for induction in view of postdates
- The most widely used index of cervical ripeness is the Bishop's score. If the Bishop's score is 6 or less, preinduction ripening will be required
- Mechanical methods, such as laminaria tents, balloons and EASI are effective at ripening the cervix
- Dinoprostone (prostaglandin E2) and misoprostol (prostaglandin E1) are used for ripening the cervix as well

as induction of labor. They carry risks of hyperstimulation, fetal heart rate abnormalities and increased risk of uterine rupture in patients with prior cesarean

- Parenteral administration of oxytocin is effective at inducing labor, especially when combined with artificial rupture of the membranes
- The safest and most widely used regimens for induction with intravenous oxytocin commence at 1 to 2 mU/min and increase the dose by 1 to 2 mU/min every 30 to 40 minutes until contractions are effective (with a contraction frequency of no more than 5 in 10 minutes). Majority of women will achieve satisfactory uterine activity with less than 16 mU/min. Less than 10% of women will require higher doses
- The labor should be closely monitored throughout for evidence of hypertonus, fetal heart rate abnormalities and progress by charting a partograph once the patient enters active phase.

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