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PROTOCOLS
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FOGSI-ICOG 2018

INDUCTION OF LABOUR:
Good Clinical Practice Recommendations

ICOG - Chairperson
Dr. S. Shantha Kumari

FOGSI - President
Dr. Jaideep Malhotra

ICOG - Editor-in-Chief
Dr. Ashok Kumar

ICOG - Secretary
Dr. Parag Biniwale

Indian College of Obstetricians & Gynaecologists The Federation of Obstetric & Gynaecological Societies of India
C-5,6,7,12,13, 1st Floor, Trade World, D-wing Entrance, S. B. Marg, Kamala City, Lower Parel (W), Mumbai - 400013.

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MESSAGE FROM PRESIDENT, FOGSI

Dr. Jaideep Malhotra

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Member, FIGO Working Group on RDEH (Reproductive & Developmental Environmental Health)

"The problems are solved, not by giving new information, but by arranging what we have known since long."

Ludwig Wittgenstein

Dear Fogsians,

In this modern era of science and technology, we are flooded with information just at a click of one button; however, such information cannot be used to treat our patients unless it is backed up with strong evidence. Developing good clinical practice guidelines that enlighten practitioners and patients is an exceptionally challenging task. It helps to improve the methods of prevention, diagnosis, treatment and clinical management. It also helps to reduce clinically significant variations among physicians in the particular management and procedures utilised in making diagnoses and providing treatment. These guidelines should be clinically valid and reliable and the content should be stated with clarity. One such field in obstetrics that requires revision and review of the available practices is induction of labour.

Over the past few decades, there has been an increase in the incidence of caesarean sections. With the increasing trend towards advanced gestational age, the increasing order of gestation and an increasing number of elective inductions, the rates of a primi section has increased. There are different and newer methods of induction available, to choose the most suitable method is of utmost clinical relevance. The timing of induction is the second most important factor responsible for a favourable pregnancy outcome. With all these updates and evidences, there is a need to develop good clinical practice guidelines in Indian scenario. With the inputs from expert obstetricians across different parts of the country, 'Good clinical practice recommendations' (GCPR) on 'Induction of labour' have been formulated.

I hope the GCPR will be of clinical help to all and will eventually help in improving the maternal outcome.

Dr. Jaideep Malhotra
President, FOGSI - 2018

MESSAGE FROM CHAIRPERSON, ICOG

Dr. S. Shantha Kumari
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Organizing Secretary AICOG 2011

Chairperson MNNRRC 2008

The ultimate outcome of good Obstetric care is the delivery of a healthy baby with a healthy mother. A fact that sounds so simple is actually a coveted aim achieved only after meticulous planning of antenatal care and delivery. There are times when the benefits of delivery outweigh the continuation of pregnancy and the need for "induction of labour" arises. This process of induction of labour (IOL) requires a comprehensive assessment of the indication, appropriate choice of the method and skilful execution to attain the final goal of obstetrics. Over the years, as Obstetric techniques have advanced and the spectrum of obstetric services has increased there has been much debate and deliberation on the increasing interventions in Obstetrics and due concern has been raised about the alarming rise in caesarean deliveries almost all across the globe. Induction of labour is also one such potential technique which can be questioned for its appropriateness as an unnecessary interference with a natural process unless we can present a viable justification for it. This edition of the ICOG newsletter has been therefore dedicated to the important topic of "Protocols in Induction of labour" so that it summarily presents the pros and cons of Induction of labour and clarifies the need for this intervention to minimize the associated perinatal morbidity and mortality if the pregnancy continues. If a delivery has to be aeffected before the actual onset of natural labour, a good induction protocol will help avoid the need for a caesarean section and hence reduce the CS rates in avoidable indications. The agents used for IOL have also seen paradigm shifts and despite the effectiveness of prostaglandins, there has been a resurgence in recent times of mechanical methods which have been refined with a better understanding of the physiology and biochemistry of the genital tract. I hope the readers will enjoy reading the recent advancements in IOL and realise that this is a powerful technique in Obstetrics - on the same note I wish to remind the young readers particularly that with power comes responsibility - so while you have a great technique at your disposal, it is in your best interests to use it justifiably, in adherence to standard protocols and for the benefit of your patient in true earnest. The ICOG stands for developing Good Practice guidelines and I strongly believe that good clinical practices applied to procedures like IOL will make a difference to help reduce the burden of "unindicated" CS deliveries and reduce maternal morbidity and mortality rates.

"Gain new knowledge by reviewing old"-analects of Confucius

Knowledge is power and path to success and the best outcomes.
Happy reading

Dr. S. Shantha Kumari
Chairperson, ICOG - 2018

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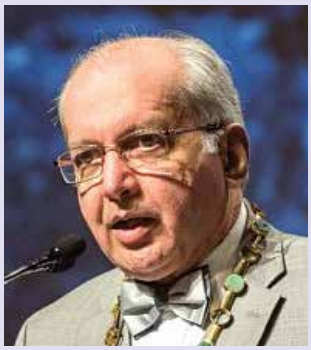

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Good Clinical Practice Recommendations: Induction Of Labour (3 June 2018)

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Good Clinical Practice Recommendations: Induction Of Labour

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METHODOLOGY

- The President FOGSI and Chairperson ICOG, 2018 realised the need of evidence-based guidelines for induction of labour for the country for uniform clinical practice to be used by obstetric care providers.
- FOGSI-ICOG GCPR (Good Clinical Practice Recommendation) development group was constituted.
- It included professors and clinicians from ICOG governing council and FOGSI.
- The priority areas were identified and a list of questions and component to answer induction of labour was prepared.
- Each member of the group performed published literature search for scientific and good quality evidences to draft a document based on each component of induction of labour.
- The documents were reviewed initially by Chairperson, Vice Chairperson, Secretary and Editor, ICOG for its uniformity and then peer reviewed by each member of the group.
- All members prepared their opinion and recommendations based on the draft document and their independent search for available evidences.
- A meeting was held on 3rd June 2018 at Gurugram. All members came prepared with their document and comments on the document prepared by other members.
- All members deliberated each component in detail and discussed comments and suggested recommendations to arrive at a consensus.
- Prior to the meeting, the core group had prepared a preliminary document containing the draft recommendations. The statements were modified or added in the meeting itself, keeping in mind the vast and varied nature of the country and locally available resources.
- The GCPR document was read again, finalised and approved by all the members of the development group at the meeting.
- After the meeting, the core group checked and edited the document.
- The document was finally approved by Chairperson, ICOG and President, FOGSI.

GOOD CLINICAL PRACTICE RECOMMENDATIONS FOGSI - ICOG 2018 INDUCTION OF LABOUR: GCPR

The participants in the GCPR Development Group agreed on the following statements that apply to all recommendations contained in these guidelines:

1. GENERAL CONSIDERATIONS

- Induction of labour should be performed only for a specific medical and/or obstetric indication.
- Expected benefits of shortening the duration of pregnancy should outweigh the potential harm from the continuation of pregnancy with no contraindications for vaginal delivery.
- The indication and process of induction of labour should be discussed with the patient.
- The profile of the patient, medical or surgical conditions, rupture of membranes, scar on the uterus, cervical status, the specific method of induction of labour and associated local resources in terms of health personnel, drugs and equipment should be taken into consideration.
- Induction of labour should be done after obtaining informed written consent.

2. SETTING FOR INDUCTION OF LABOUR

- All patients should be admitted for induction of labour in a health facility having facilities for caesarean section and management of complications.
- Induction of labour should be done under necessary supervision.
- Maternal and foetal monitoring should be done and the progress of labour should be documented.

3. PREREQUISITES & PREINDUCTION ASSESSMENT

- Informed written consent.
- Review of maternal history and profile.
- Evaluation for indications and rule out any contraindications.
- Reliable estimation of gestational age, presentation and foetal weight.
- Maternal pulse, blood pressure, temperature, respiratory rate and findings on abdominal palpation must be recorded.
- Evaluation of baseline foetal heart rate pattern by auscultation/electronic foetal monitoring.
- Maternal pelvis assessment and clinical evaluation for possible cephalopelvic or feto-pelvic disproportion.
- Assessment of cervical status using modified Bishop scoring system to predict the likelihood of success and select appropriate method of induction of labour.
- Indication for induction of labour and gestational age along with modified Bishop Score should be documented at the time; the decision for induction of labour is made.

Cervix	Score				Bishop Score Modifiers
	0	1	2	3	
Cervical Dilation (cm)	0	1-2	3-4	5+	**Add 1 point for:** -Preeclampsia -Each previous vaginal delivery
Cervical Length (cm)	>4	2-4	1-2	<1	
Station of Presenting Part (cm in relation to ischial spine)	-3 or above	-2	-1,0	+1, +2	**Subtract 1 point for :** -Postdate pregnancy -Nulliparity -PPROM
Consistency	Firm	Medium	Soft		
Position	Posterior	Midposition	Anterior		

Total score: 13; Favourable Score: 6 - 13; Unfavourable Score: 1 - 5

4. INDICATIONS, CONTRAINDICATIONS AND TIMING

4.1. Induction of labour for a low-risk pregnancy is recommended to be carried out only after 39 weeks.

- At 39 weeks in low-risk nulliparous women, induction of labour results in a lower frequency of caesarean delivery without a statistically significant change in the frequency of a composite of adverse perinatal outcomes.[1]

4.2. There could be some specific conditions in the mother or in the foetus that can mandate induction of labour.

4.2.1.Term Pre-Labour Rupture of Membranes

- Induction of labour is recommended if there is prelabour rupture of membranes (PROM) at more than 37 weeks.
- Initial assessment of women presenting with term PROM involves confirmation of the diagnosis, gestation age, presentation and assessment of maternal and foetal well-being.
- Active management of term PROM with induction is associated with reduced maternal infective morbidity and increased maternal satisfaction without increasing caesarean section or operative vaginal birth. Fewer infants are admitted to NICU and fewer infants require postnatal antibiotics.[2,3]

4.2.2. Hypertensive Disorders in Pregnancy

- For women with preeclampsia, induction should be planned at 37 weeks or earlier if indicated for maternal or foetal compromise.
- For women with gestational hypertension at low risk of adverse outcomes, expectant management can be considered beyond 37 weeks.
- Induction of labour is associated with improved maternal outcome and should be advised for women with mild hypertensive disease beyond 37 weeks and 39 weeks gestation. In women with preeclampsia or gestational hypertension beyond 34 weeks of gestation, elective delivery can decrease the incidence of complications, severe hypertension and the need for antihypertensive drug therapy.[4–6]

4.2.3. Diabetes in Pregnancy

- Induction of labour is not recommended before 39 weeks in a woman with gestational diabetes mellitus well controlled on diet.
- Induction of labour is recommended at 38 weeks of gestation if diabetes is controlled on insulin/oral hypoglycaemics.
- Management of women with uncontrolled diabetes should be individualized.
- In women with gestational diabetes, without other maternal or foetal conditions, no difference was detected in birth outcomes regardless of the approach used (i.e., induction between 38 and 39 weeks vs. expectant management).[7-9]

4.2.4. Foetal Growth Restriction

- Induction of labour at term is advisable for foetal growth restriction to prevent still birth.
- The timing however, is guided by the severity of foetal growth restriction and any deterioration in the Doppler parameters during intensive foetal monitoring.

4.2.5. Twin Pregnancy

- In uncomplicated twin pregnancy, where there are no contraindications to vaginal delivery, induction of labour at 37 weeks is advisable.
- Contraindications of induction of labour in twin pregnancy are mono-amniotic twins and first twin non-cephalic.
- Early birth at 37 weeks and 39 weeks gestation compared with ongoing expectant management for women with an uncomplicated, dichorionic twin pregnancy does not appear to be associated with an increased risk of harm.[10]

4.2.6. Obstetric Cholestasis (Intrahepatic Cholestasis of Pregnancy)

- Induction should be considered between 37 and 38 weeks to improve perinatal outcome.
- An earlier induction (around 36 weeks) may be warranted in the presence of severe biochemical abnormalities especially severe derangements of bile acids levels.

4.2.7. Intrauterine Foetal Demise

- The woman and her partner should be supported and counselled to cope with the situation.
- Woman should be offered a choice of immediate induction of labour or expectant management. However in the presence of conditions like sepsis, preeclampsia or abruption, immediate delivery should be planned.
- Although most patients will desire prompt delivery, immediate delivery is not critical. In more than 90% of the women, labour starts spontaneously in 3 weeks of diagnosis.[11]
- Disseminated intravascular coagulopathy has been reported in 25% of women who retain a dead foetus for more than 4 weeks.[12]
- If induction is delayed for more than 48 hours, woman should have testing for disseminated coagulation failure twice a week.
- For induction of labour, PGE2 and oxytocin can be used.
- The use of misoprostol is off label (Appendix B).

4.2.8. Previous Caesarean Section

- The essential prerequisite for the induction of labour in a woman with previous caesarean is the availability of facilities for maternal-foetal monitoring and emergency caesarean section.

- A detailed review of patient clinical profile should be done to ensure the eligibility for a vaginal delivery.
- Counselling should be done conveying the chances of vaginal delivery and the risk of uterine rupture with the use of various agents for induction of labour.
- In general, at least 60% of the inductions result in a vaginal delivery in women with previous caesareans[13] and the number may be much higher in women with a favourable cervix and a previous vaginal delivery.
- Although the chances of uterine rupture are increased with induction of labour, the absolute risk is still reasonably low.
- In women with favourable cervix , amniotomy followed by oxytocin infusion is advisable
- In women with unfavourable cervix, use of mechanical methods like transcervical Foley catheter is the preferred method for induction of labour, followed by amniotomy and oxytocin.
- The use of prostaglandins is contraindicated for use in women with a scarred uterus because of a high risk of uterine rupture.

4.2.9. Preterm Prelabour Rupture of Membranes

- If preterm prelabour rupture of membranes occurs after 34 weeks, the plan for induction should be made after discussing with the women the risks of sepsis to the woman and to the baby, complications of preterm birth and availability of neonatal intensive care facilities.
- If preterm prelabour rupture of membranes occurs after the period of viability, induction of labour should not be carried out before 34 weeks, unless there are additional obstetric indications (chorioamnionitis or foetal compromise).
- Antenatal steroids and antibiotics should be administered as appropriate.
- Magnesium sulphate for neuroprotection should be considered if delivery happens before 32 weeks.
- Tocolysis is not recommended as it does not significantly improve outcome. It may be given to delay delivery till the effects of steroids occur.

4.3. Contraindications of Induction of Labour

Induction should be avoided if there are any contraindications to labour or vaginal delivery which can be because of:

- Placenta or vasa previa
- Umbilical cord presentation
- Transverse lie or footling breech
- Prior classical or inverted T uterine incision
- Significant prior uterine surgery (e.g., full-thickness myomectomy, transfundal uterine surgery)
- Active genital herpes
- Pelvic structural deformities associated with cephalopelvic disproportion
- Invasive cervical carcinoma
- Previous uterine rupture
- Previous pelvic surgeries like vesicovaginal fistula/rectovaginal fistula/pelvic floor repair (third or fourth degree perineal tears repair), trachelorrhaphy

5. METHODS OF CERVICAL RIPENING AND INDUCTION OF LABOUR IN UNFAVOURABLE CERVIX

5.1. Prostaglandins E2

- Prostaglandins (PG) E2 (dinoprostone) is available in two forms in India for cervical ripening.
  i) Dinoprostone gel (3 g gel/0.5 mg dinoprostone) is placed inside the cervix, but not above the internal os. The application can be repeated after 6-8 hours, not to exceed 3 doses in 24 h.

  ii) Dinoprostone vaginal pessary (10 mg embedded in a mesh) is placed transversely in the posterior fornix of the vagina for 24 h.

- PGE2 has an associated risk of uterine tachysystole and higher rates of chorioamnionitis in the setting of ruptured membranes.

- The use of vaginal and intracervical dinoprostone may not be very effective in women with ruptured membranes.

- Both forms are found to have equal efficacy. Both result in a significantly lower caesarean delivery rate and an increased proportion of vaginal deliveries within 24 h.[14,15]

- Vaginal preparations are easier to administer than the intracervical preparation.

5.1.1 Intracervical Dinoprostone Gel

- The gel should be stored in a refrigerator at '2° to 8°C'.

- The application (3 g gel/0.5 mg dinoprostone) can be repeated in 6 h, not to exceed three doses in 24 h.

- Ambulation of the patient is allowed after 30 min of insertion

- Temperature, pulse, respiratory rate, blood pressure, uterine activity and vaginal bleeding should be examined immediately after insertion then hourly for 4-6 h.

- If necessary oxytocin for augmentation of labour is started only 6 h after the last dose.

5.1.2. Dinoprostone Vaginal Pessary

- The dinoprostone pessary (10 mg), placed transversely in the posterior fornix of the vagina, releases PGE2 at a constant rate of approximately 0.3 mg/hour over the 24-h dosing period.

- Ambulation of the patient is allowed after 30 min of insertion.

- Monitoring at frequent intervals for uterine contractions and foetal condition should begin after administration of the drug.

- It is removed at the end of the 24-h dosing period or once the onset of active labour is achieved, whichever is earlier.

- Rupture of membranes after the insertion of pessary does not necessitate removal of the pessary.

- It can be easily administered and quickly removed in case of uterine hyperstimulation.

- Oxytocin for augmentation of labour, if necessary is started 30 min after the removal of the pessary.

- The pessary should be stored in a freezer at' -10° to -25°C'.

5.1.3. Prostaglandin PGE1 (Misoprostol)

- Misoprostol is not yet approved for induction of labour by Drug Controller General of India.

5.2. Balloon Devices: Foleys Catheter

- Transcervical Foleys catheter is safe, cheap, easy to store and preferred in cases of scarred uterus and unfavourable cervix provided there are no signs of infection.
- It causes less uterine hyperstimulation as compared to prostaglandins but does not reduce caesarean rates.[16,17]
- Balloon catheter and vaginal prostaglandins may have similar effectiveness.
- A small degree of traction on the catheter by taping it to the inside of the leg.
- The catheter is left in place until it falls out spontaneously or for 24 h.
- Foleys catheter followed by oxytocin infusion is recommended as an alternative method for induction of labour.
- It is contraindicated in placenta previa and should be avoided in women with ruptured membranes and undiagnosed vaginal bleeding.

5.3. Low-Dose Oxytocin Infusion

- The low-dose regimen for cervical ripening begins with 1 to 2 mU/min, increased to1 to 4 mU at every 30-min interval. It can be used in patients where prostaglandins are not available.
- Infusions pump, wherever available should be used.
- Oxytocin should be stored in refrigerator at' 2° to 8°C '.

5.4. Membranes Sweeping

- It solely improves rate of entering spontaneous labour. It does not improve maternal or neonatal outcome improvements.[18]
- It is suitable for non-urgent indications for term pregnancy termination because interval between sweeping membranes and initiation of labour can be longer than other methods of cervical ripening.
- It can be done simultaneously at the time of assessing the cervix after informing the patient.
- It can be repeated if labour does not start spontaneously.

5.5. Other Methods

- Hygroscopic dilators (laminaria tents), mifepristone, nitric oxide donors, relaxin, hyaluronidase or breast nipple stimulation are presently not recommended for induction of labour in view of the availability of low quality evidence for their use.

6. INDUCTION OF LABOUR WITH A FAVOURABLE CERVIX

6.1. Oxytocin

- Intravenous oxytocin is the most commonly used method of induction for women with a favourable cervix (Modified Bishop Score >6).
- Oxytocin can be used alone, in combination with amniotomy, or following cervical ripening. It can be used for induction as well as augmentation of labour.
- It should be used with caution in women with previous caesarean delivery and grand multiparous women because of the risk of uterine rupture.
- Intravenous oxytocin and amniotomy is most likely to achieve vaginal delivery in 24 h.
- Oxytocin should be administered intravenously as an infusion to allow continuous, precise control of the dose administered.
- The low-dose regimen begins with 1 to 2 mU/min, increased incrementally by 1 to 2 mU at every 30-min intervals.
- The high-dose regimen starts with 4 to 6 mU/min with dose increments of 4 to 6 mU/min every 15 to 30 min.
- High dose protocols reduce the induction delivery interval and are associated with higher rates of tachysystole than low dose protocols. Maternal and foetal complication rates are similar with both protocols.
- Infusion of oxytocin should be documented in mU/min or drops/min with the dilution being mentioned.
- The oxytocin infusion can be increased until labour progress is normal or uterine activity reaches 200 to 250 Montevideo units (i.e., good regular uterine contractions, each lasting for 40–45 seconds duration and minimum of three contractions in 10 min).
- Upper limit of the oxytocin infusion during labour with a live foetus in the third trimester is 40 mU/minute.
- Monitoring for infusion rate of oxytocin and uterine contractions and foetal heart rate by continuous cardiotocography is preferable.
- In facilities where cardiotocography is not available, foetal monitoring should be done by intermittent auscultation every 15 min in first stage and 5 minutes in second stage.
- Blood pressure and pulse should be assessed every hour. Intake and output should be assessed every 4 h. The frequency, intensity and duration of uterine contractions should be assessed every 30 min and with each incremental increase in oxytocin.
- Cervical status should be assessed prior to administration of oxytocin and repeated after at least 4 hours of moderate contractions.
- A vaginal examination may also be repeated in situation of a non-reassuring foetal heart pattern to rule out the presence of meconium, abruption or a cord accident.
- Close watch is kept for clinical features of maternal hyponatremia, uterine hyperstimulation and uterine rupture.

Preparation of Oxytocin Infusion and Dose Calculation

- Oxytocin is administered as dilute solution by intravenous route. Isotonic solutions such as ringer lactate or normal saline are preferred over dextrose solution for fluid selection to minimize the risk of electrolyte imbalance (e.g. hyponatremia) and volume overload.
- Each ampoule (1 ml) of oxytocin contains five units.
- 2 ml of oxytocin (two ampoules) is taken in a 10 ml syringe and diluted with 8 ml of normal saline. It makes 10 ml of saline solution having 10 units of oxytocin. **1 ml of this saline solution contains 1unit of oxytocin.** To make a bottle of 2 units of oxytocin infusion, 2 ml of this solution is added in 500 ml of Ringer Lactate.

  The dose of oxytocin in drops/minute and mU/minute is shown below:-

Units of Oxytocin added in 500 ml of Ringer Lactate	Oxytocin infusion in Drops per minute & equivalent dose in mU/minute (1 ml is equal to 16 drops)							
1 Unit	8 Drops	16 Drops	24 Drops	32 Drops	40 Drops	48 Drops	56 Drops	64 Drops
	1mU	2mU	3mU	4mU	5mU	6mU	7mU	8mU
2 Unit	8 Drops	16 Drops	24 Drops	32 Drops	40 Drops	48 Drops	56 Drops	64 Drops
	2mU	4mU	6mU	8mU	10mU	12mU	14mU	16mU

6.2. Amniotomy

- A simple and effective method when the membranes are accessible and the cervix is favourable. It creates a commitment to delivery.
- Flow of amniotic fluid should be controlled with vaginal fingers. The liquor should be drained slowly because sudden decompression of uterus can lead to placenta abruption.
- Care should be taken when amniotomy is done in unengaged presentation because there is a risk of cord prolapse. The vaginal fingers should not be removed until presenting part rests against the cervix.
- Amount and colour (meconium or blood stained) of the liquor is observed.
- Monitoring of foetal heart should be done during and after the procedure.
- Amniotomy alone is not recommended for induction of labour.
- Oxytocin should be commenced immediately after amniotomy or after two hours depending on the intensity of uterine contractions.

7. MONITORING DURING INDUCTION OF LABOUR

- Maternal and foetal monitoring is a must.
- Before induction of labour, a non-stress test is recommended.
- Intermittent maternal and foetal (foetal heart rate) monitoring should be done every hour initially.
- Continuous electronic/more frequent intermittent foetal heart rate monitoring should be started in active labour
- Progress of labour is monitored using partogram.
- Close watch is kept for temperature, pulse rate, blood pressure, foetal heart pattern, vaginal bleeding, uterine hyperstimulation, uterine rupture and scar dehiscence in women with previous caesarean delivery.

8. PAIN RELIEF

- Women should be informed of the availability of pain relief options.
- Women should be provided pain relief appropriate for them after counselling. This can range from simple analgesics to epidural analgesia.
- Women should be encouraged to use breathing and relaxation techniques in labour.
- There is no need to wait for labour analgesia arbitrarily till the cervical dilation has reached 4–5 cm.[19,20]
- If given early in labour, it does not affect the progress of labour.[21]
- Pethidine and opioid analgesia can be used for short term pain relief, preferably in early labour.
- If regional analgesia is planned, the woman should be informed about the risks and benefits and the implications for her in labour.

9. COMPLICATIONS OF INDUCTION OF LABOUR

9.1. Uterine Hyperstimulation

- First step is to discontinue oxytocin infusion or withdraw dinoprostone vaginal pessary.
- Tocolytics preferably betamimetics are recommended for women with uterine hyperstimulation during induction of labour. Contraindications of betamimetics especially cardiac disease should be kept in mind.
- If associated with abnormal foetal heart pattern, delivery should be accomplished.

9.2. Uterine Rupture

- Rupture can occur in both scarred and unscarred uterus and is associated with multiparity, malpresentation, unsupervised or aggressive use of uterotonics.
- Woman with previous caesarean undergoing induction of labour should be counselled.
- A close watch is kept on maternal signs and monitoring is done for foetal heart rate abnormality.
- In suspected case of uterine rupture or scar dehiscence, delivery is by emergency caesarean section.

9.3. Failed Induction

- Failed induction of labour must be differentiated from failure of labour progress.(Appendix)
- Maternal and foetal well-being should be reassessed.
- Subsequent management options are:

  i. Another attempt to induce labour with a different method can be considered after discussion with the patient but it depends on the nature and urgency of the clinical situation (indication of the induction of labour)

  ii. Caesarean delivery.

10. COUNSELLING OF WOMEN PLANNED FOR INDUCTION OF LABOUR

- The information should be provided to the patient and her partner before the process of induction is planned (Appendix C)
- The woman should be given enough time to discuss and ask any questions.
- It should include the following:

  i. Indication of induction of labour

  ii. Risks vs benefit of induction of labour

  iii. Method of induction of labour and its advantages and disadvantages

  iv. Any alternatives available

  v. Use of electronic equipment for monitoring

  vi. Expected duration of labour

  vii. Support system available during labour

  viii. Pain relief

  ix. Option available if induction of labour fails

11. MATERNAL REQUEST FOR INDUCTION OF LABOUR

- The maternal request for induction of labour at term for nonmedical reasons should not be entertained as it is an unnecessary intervention except under exceptional circumstances.

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APPENDIX A

DEFINITIONS

Induction of labour: Artificial initiation of contractions in a pregnant woman who is not in labour to help her achieve a vaginal birth within 24 to 48 h. Successful induction: A vaginal delivery within 24 to 48 h of induction of labour.

Elective induction: Induction of labour in the absence of acceptable foetal or maternal indications.

Cervical ripening: Use of pharmacological or other methods to soften, efface, or dilate the cervix to increase the likelihood of a vaginal delivery.

Tachysystole: More than five uterine contractions in 10-min period averaged over 30 min. This is further subdivided into two categories, one with and one without foetal heart rate changes.

Hypertonus: Excessive uterine contractions lasting more than 120 seconds without fetal heart rate changes.

Hyperstimulation: Excessive uterine contractions (tachysystole or hypertonus) as a result of induction of labour with nonreassuring foetal heart rate changes.

Amniotomy: Artificial rupture of the membranes to initiate or speed up labour.

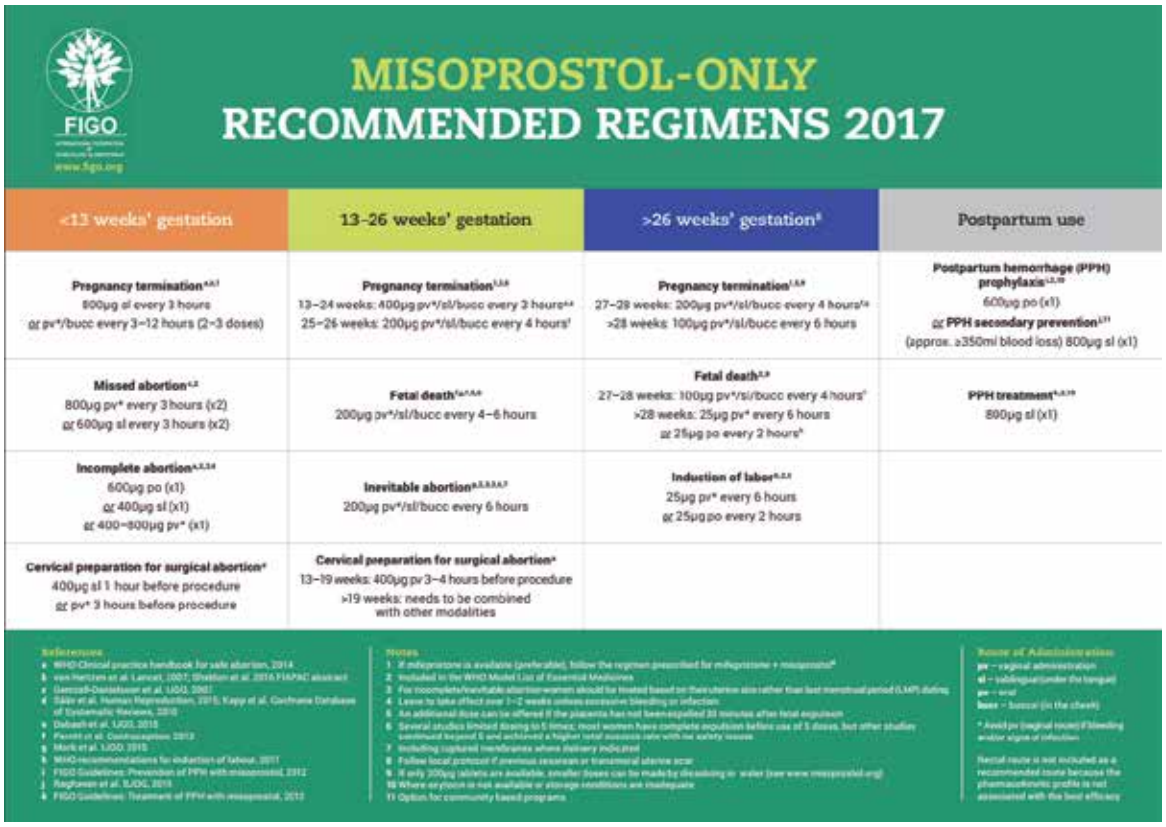
Analgesia: Pain relief without loss of consciousness.

Failed induction: Failure to achieve regular uterine contractions (every 3 minutes) after one cycle of completion of cervical ripening consisting of

(a) Insertion of three intracervical PGE2 gel (3g) at 6-h intervals, and 12 h of oxytocin administration after rupture of membranes, if feasible, or

(b) One PGE2 pessary (10 mg) within 24 h

APPENDIX B



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MISOPROSTOL-ONLY RECOMMENDED REGIMENS 2017

<13 weeks' gestation	13–26 weeks' gestation	>26 weeks' gestation[8]	Postpartum use
Pregnancy termination[4,6,7] 800µg sl every 3 hours or pv*/bucc every 3–12 hours (2–3 doses)	**Pregnancy termination**[1,3,8] 13–24 weeks: 400µg pv*/sl/bucc every 3 hours[4,6] 25–26 weeks: 200µg pv*/sl/bucc every 4 hours[1]	**Pregnancy termination**[1,3,8] 27–28 weeks: 200µg pv*/sl/bucc every 4 hours[1,6] >28 weeks: 100µg pv*/sl/bucc every 6 hours	**Postpartum hemorrhage (PPH) prophylaxis**[1,2,10] 600µg po (x1) or **PPH secondary prevention**[2,11] (approx. ≥350ml blood loss) 800µg sl (x1)
Missed abortion[4,5] 800µg pv* every 3 hours (x2) or 600µg sl every 3 hours (x2)	**Fetal death**[1a,1,3,8] 200µg pv*/sl/bucc every 4–6 hours	**Fetal death**[3,8] 27–28 weeks: 100µg pv*/sl/bucc every 4 hours[1] >28 weeks: 25µg pv* every 6 hours or 25µg po every 2 hours[9]	**PPH treatment**[8,9,10] 800µg sl (x1)
Incomplete abortion[4,5,14] 600µg po (x1) or 400µg sl (x1) or 400–800µg pv* (x1)	**Inevitable abortion**[4,5,8,8A,9] 200µg pv*/sl/bucc every 6 hours	**Induction of labor**[8,12] 25µg pv* every 6 hours or 25µg po every 2 hours	
Cervical preparation for surgical abortion[4] 400µg sl 1 hour before procedure or pv* 3 hours before procedure	**Cervical preparation for surgical abortion**[4] 13–19 weeks: 400µg pv 3–4 hours before procedure >19 weeks: needs to be combined with other modalities		

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e Debaeh et al. IJOG, 2010
f Parent et al. Contraception 2013
g Mork et al. IJOG 2015
h WHO recommendations for induction of labour, 2011
i FIGO Guidelines: Prevention of PPH with misoprostol, 2012
j Raghavan et al. BJOG, 2013
k FIGO Guidelines: Treatment of PPH with misoprostol, 2012

Notes

1 If mifepristone is available (preferable), follow the regimen prescribed for mifepristone + misoprostol[4]
2 Included in the WHO Model List of Essential Medicines
3 For incomplete/inevitable abortion women should be treated based on their uterine size rather than last menstrual period (LMP) dating
4 Leave to take effect over 1–2 weeks unless excessive bleeding or infection
5 An additional dose can be offered if the placenta has not been expelled 30 minutes after fetal expulsion
6 Several studies limited dosing to 5 times; most women have complete expulsion before use of 5 doses, but other studies continued beyond 5 and achieved a higher total success rate with no safety issues
7 Including ruptured membranes where delivery indicated
8 Follow local protocol if previous cesarean or transmural uterine scar
9 If only 200µg tablets are available, smaller doses can be made by dissolving in water (see www.misoprostol.org)
10 Where oxytocin is not available or storage conditions are inadequate
11 Option for community based programs

Route of Administration

pv = vaginal administration
sl = sublingual (under the tongue)
po = oral
bucc = buccal (in the cheek)

* Avoid pv (vaginal route) if bleeding and/or signs of infection

Rectal route is not included as a recommended route because the pharmacokinetic profile is not associated with the best efficacy

Source: https://www.figo.org

APPENDIX C

GOOD CLINICAL PRACTICE GUIDELINES FOGSI - ICOG 2018 INDUCTION OF LABOUR: GCPR

PATIENT INFORMATION SHEET

Name of patient: .....w/o:.....

ID No.....

This information sheet provides you with the details of the procedure. You are requested to go through the document carefully. In case of any query/ doubt, you should talk to your doctor for a further explanation. After reading and understanding the document, you will need to sign the document.

What does Induction of Labour mean?

Induction of labour is a process where the uterine contractions are artificially initiated to start the procedure of childbirth to achieve a vaginal delivery.

Why is it needed?

Induction of labour may be offered for various reasons where your doctor feels that delivering the baby would be more beneficial for the mother and child than continuing the pregnancy.

In your case, induction of labour is being done for:

Diagnosis:.....

Indication:.....

What are the success rates?

Induction of labour does not necessarily mean that the patient will have a vaginal delivery. The success of induction depends upon many factors including a previous normal delivery, the condition of the cervix and position of the head of the baby. If unsuccessful, a reevaluation would be done to decide if a further trial can be given or it is better to go for a caesarean section.

Preparation:

Induction of labour is done after admission to the hospital where both the mother and the baby can be monitored.

Complications:

- **Failed induction:** Induction of labour may not result in the initiation of the labour or the labour might get initiated but does not result in vaginal birth and might need caesarean delivery.
- **Hyperstimulation:** Prostaglandins and oxytocin may lead to hyperstimulation of the uterus (excessive uterine contractions)
- **Nausea, vomiting and diarrhoea:** Some women tend to have gastrointestinal side effects with the prostaglandins.
- **Uterine Rupture:** There is an occasional chance of uterine rupture, although very rare, especially in women who have had previous uterine surgery or cesarean section.
- **Infection:** Mechanical methods are associated with the risk of maternal infection. Women who undergo induction of labour after the membranes have ruptured are at increased risk of infection.
- **Cord accident:** Amniotomy has be associated with the risk of cord prolapse and need for emergency Caesarean section
- **Foetal heart rate abnormalities:** Induction of labour can be associated with foetal heart rate changes and need for an emergency caesarean section.

CONSENT FORM

I (Name of the patient)wife of Sh. (Name of the Husband)

ID No: .....

have read the above document and have understood the need for the proposed procedure. The indication, possible complications and need for further procedure in case of failure of the induction of labour has been explained to us by our doctor (Name of the doctor).
I have been given the opportunity to ask questions and clarify my doubts.

I hereby give my full consent to undergo the procedure. I understand the risk involved.

Procedure (specify the method of induction of labour):

Indication:

Time and date: Place:

Name & signature of the patient Name and signature of the attendant

Name & signature of the doctor Name & signature of the witness

APPENDIX D

CHECK LIST

Method used for the patient:.....

Name of patient: ..... w/o: .....

ID No.....; Date:.....; Time:.....

Age (Date of birth) : ..... years; Gravida & parity : .....

LMP (last menstrual period) : .....

Expected date of delivery :.....

Corrected Expected date of delivery: .....

Gestational age by LMP : .....

Gestational age by first ultrasound (done before 20 weeks of gestation) :.....

History of any allergies, medical condition , special need: Yes/ No

High Risk Review: Yes/No

Indication for Induction Reviewed : Yes/ No

Planned Method of Induction: Yes/ No

Consent form signed by the patient and her attendant : Yes/ No

Foetal Heart Rate Assessment :Yes/ No

Pre-Induction Modified Bishop's Score:

Score	Cervical dilatation (cm)	Position of cervix	Cervical consistency	Cervical Length (cm)	Station
0	Closed	Posterior	Firm	>4	-3
1	1-2	Central	Medium	3-4	-2
2	3-4	Anterior	Soft	1-2	-1,0
3	5-6	-	-	<1	+1.+2

- Total Score of the patient: .....; (Favourable Score: 6-13 & Unfavourable Score: 0-5)

Signatureof the Doctor:.....; Date and time:.....

Name of the Doctor:.....

INTRODUCTION: NEED OF GUIDELINES FOR INDUCTION OF LABOUR

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"A guideline is a description of the process of care which will permit health to improve, and which has the potential of improving the quality of medical decisionmaking".[1]Practice guidelines are systematically developed statements to assist practitioner and patient decisions about appropriate health care for specific clinical circumstances. Formulation of guidelines undergoes through three basic stages: development, intervention and evaluation. The second and third stage ideally involves feedback to the first stage to prompt the revision of guidelines whenever problems are identified in the procedure or technique. Thus guidelines are dynamic and not static they need to be modified according to the scientific and technological progress. The attributes of Good Clinical Practices (GCP) are validity, reliability/reproducibility, clinical applicability, clinical flexibility and clarity.[1,2]

Induction of labour (IOL) seeks to advance a process which in the natural course of the event is inevitable. IOL is intended to achieve vaginal delivery by stimulating uterine contractions before its spontaneous onset, and is commonly performed in clinical practice. Generally, it is considered as a therapeutic option when the outcome of pregnancy will be better if it is artificially interrupted rather than being left to follow its natural course. In addition, local resources, preference and profile of the woman, cervical status and associated medical and obstetric conditions are also taken into account. Since IOL is associated with the risk of uterine stimulation leading to foetal distress and uterine rupture, it should be carried out in facilities where maternal and foetal wellbeing can be monitored and caesarean section can be performed.[3]

Over the past decades, more and more pregnant women around the world have undergone induction of labour to deliver their babies. In developed countries, up to 25% of all deliveries at term, now involve induction of labour. In developing countries, the rates are generally lower, but in some settings, they have been found to be as high as 30%.[4] However, lack of reporting and auditing may influence these figures. The World Health Organization (WHO) recommends induction to be performed with a clear medical indication and when expected benefits outweigh potential harms.[3] The WHO Global Survey on Maternal and Perinatal Health (WHOGS-2013), a multi-country, cross-sectional survey of all institutional deliveries over a 2or3-month period, has described the epidemiology and outcomes of labour induction in 192,538 deliveries in 253 facilities across 16 countries in Africa and Asia.

According to the survey, there has been a rise in the rate of inductions in both high and low resource settings, which may be attributed to patient and physician factors. Induction accounted for 4.4% (Africa) and 12.1% (Asia) of deliveries.[4] Guerra et al. reported an elective induction rate of 16.7% in Latin American facilities,[5] while the WHOGS found nearly 50% of inductions in Asian facilities were elective, driven by Sri Lanka (77.2%), Thailand (44.6%), Japan (41.0%), India (32.1%) and China (20.4%). Approximately one-third of elective inductions in African and Asian facilities occurred at less than 39 weeks of gestation.[4] Induction without medical indication accounted for less than 2% of deliveries in all countries, except for Sri Lanka (27.8%), Japan (8.5%), India (3.6%) and Thailand (3.5%).4In 2004-2005, 19.8% of all deliveries in the United Kingdom were induced. This includes induction for all medical reasons.[6]

In Asian population, the common indication for IOL was prolonged pregnancy (19.4%) followed by premature rupture of membranes (PROM) (19.3%).[4] The most common method of IOL was oxytocin followed by oxytocin and non-pharmacological methods. According to WHO guidelines, prostaglandins should be the first-line drugs for IOL; however, the use was not widespread in the Asian countries.[3] However, every attempt of IOL should also take into consideration the safety of the woman. Induction success (inductions resulting in a vaginal birth) was 83.4% in Africa and 81.6% in Asia. Medically indicated inductions were associated with increased adjusted odds of Apgar score less than 7 at 5 minutes, low-birth weight, neonatal intensive care unit (NICU) admission and fresh stillbirth in both regions. Elective induction was associated with increased adjusted odds of NICU (Africa) and ICU (Asia) admissions but not increased odds of foetal or neonatal mortality.[4] Carefully planned IOL will promote vaginal delivery, thereby improving the much needed caesarean rates.

Isolated Indian data regarding epidemiology of IOL is scarce though there are several studies available for methods of induction; however, guidelines are in need of the hour in view of the wide and large geographic region. Further research is required to study physician and patient factors contributing to the elective induction rate, cost-effectiveness, induction practices at the level of smaller facilities and the community and regional cultural practices. With all the scientific advances, the techniques should be introduced that replicate the natural childbirth process successfully and safely.

The pattern of medical indications for inductions is evolving with changing demographics and pregnancy complications. Recent advances in dynamics of labour, advanced age of conception, increasing incidence of assisted reproductive techniques and modified nomenclature of term pregnancy warrant the need to formulate guidelines specific for a given population.

The primary goal of the present guidelines is to improve the quality of care and outcomes for pregnant women undergoing induction of labour. The secondary goal is to reduce the number of operative vaginal deliveries. The target audience is obstetricians, midwives, general medical practitioners, healthcare managers and public health policy-makers. The good clinical practice recommendations are formulated keeping in mind the vast nature of the country with varied clinical practices and availability of resources. These standards will definitely go to improve the quality of health-care services.

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INDUCTION OF LABOUR: AN OVERVIEW

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Induction of labour (IOL) means initiation of uterine contractions after a period of viability (i.e., after 28 weeks) but before onset of spontaneous delivery, by any method (medical, surgical or combined) for the purpose of vaginal delivery. IOL-one of the most commonly performed obstetrical procedures in every labour room. Over recent decades, more and more pregnant women around the world have undergone IOL to deliver their babies. In developed countries, up to 25% of all deliveries at term now involve IOL. In developing countries, the rates are generally lower, but in some settings, they can be as high as those observed in developed countries. The advent of inducing agents has eased the delivery process immensely by reducing the duration of labour. The incidence of induction varies from setting to setting ranging from 5% to 22% of all labour room admissions and depends on the institutional protocol. In spite of many issues like proper indication, maternal and foetal hazards and increased incidence of caesarean section, the rate of induction is on the rise.

RELATED DEFINITIONS

- **Successful induction** is defined as a vaginal delivery within 24 to 48 hours of IOL.
- **Elective induction** is the IOL in the absence of acceptable foetal or maternal indications.
- **Cervical ripening** is the use of pharmacological or other means to soften, efface, or dilate the cervix to increase the likelihood of a vaginal delivery.
- **Tachysystole** refers to >5 contractions per 10-minute period averaged over 30 minutes. This is further subdivided into two categories, one with and one without foetal heart rate changes.
- **Hypertonus** refers to excessive uterine contractions lasting >120 seconds without fetal heart rate (FHR) changes. This term has been replaced in this guideline by tachystole without FHR changes.
- **Hyperstimulation** refers to excessive uterine contractions (tachysystole or hypertonus) with abnormal FHR changes. This term has been replaced by tachystole with FHR changes.

WHY INDUCTION OF LABOUR IS DONE?

Over the years, various professional societies have recommended the use of IOL in circumstances in which the risks of waiting for the onset of spontaneous labour are judged by clinicians to be greater than the risks associated with shortening the duration of pregnancy by induction.[1] Although currently available guidelines do not recommend this, IOL is being used more and more at the request of pregnant women to shorten the duration of pregnancy or to time the birth of the baby according to the convenience of the mother and/or health-care workers.[2]

ACCEPTED ABSOLUTE INDICATIONS OF IOL

- Hypertensive disorders: Pre-eclampsia or eclampsia and IOL according to the severity of disorder
- Maternal medical conditions: Diabetes mellitus, renal disease, chronic pulmonary disease
- Foetal compromise:-Foetal growth restriction, isoimmunization, non-reassuring antepartum foetal testing, oligohydramnios
- Pre-labour rupture of membranes: before 37 completed weeks of gestation
- Fetal demise
- Chorioamnionitis
- Prolonged pregnancy (>42weeks)

RELATIVE INDICATIONS FOR IOL

- Logistic factors: Risk of rapid labour, distance from hospital, psychosocial indications, advanced cervical dilatation.
- Polyhydramnios
- Previous still birth
- Post-term pregnancy(>41weeks)[3]

GENERAL PRINCIPLES RELATED TO THE PRACTICE OF IOL

- IOL should be done only when there is a clear medical indication and benefits outweigh its potential harms. For IOL to be considered and to be offered there must be evidence that such an intervention carries benefits for the mother and/or her baby and this requires careful consideration of the clinical evidence in discussion with the woman. When the benefits of expeditious delivery are greater than the risks of continuing the pregnancy, inducing labour can be justified as a therapeutic intervention.[4]
- The benefits, the complications and the possibility of a caesarean section should be explained.
- Consideration must be given to the actual condition, wishes and preferences of each woman, with emphasis being placed on cervical status.
- It is also imperative that the most accurate information is obtained concerning the gestational age of the pregnancy.
- IOL should be performed with caution due to risk of uterine hyperstimulation and rupture and foetal distress.
- Facilities should be available for assessing maternal and foetal well-being.
- Women receiving oxytocin, misoprostol or other prostaglandins should never be left unattended.
- Failed IOL does not necessarily indicate caesarean section, although, wherever possible, IOL should be carried out in facilities where caesarean section can be performed.

PREREQUISITES FOR IOL

- Informed and written consent.
- Maternal pelvis assessment.
- Foetal weight, presentation and gestation.
- Confirm lung maturity if possible to reduce the incidence of perinatal mortality.
- Cervical status must be assessed.
- A cervical examination is essential before labour induction is initiated and the condition of the cervix influences the success of inducing labour.
- In 1964, Bishop developed a scoring system to evaluate multiparous women for elective induction at term. The scoring system is based on properties of the cervix that may be assessed clinically at the time of pelvic examination such as dilatation, effacement, consistency, and position as well as the station of the foetal presenting part.
- Modified Bishop Score is now widely used to predict the success of labour induction. In this scoring system, effacement has been replaced by cervical length in centimetres so more easy to measure and less inter-examiner variability.
- Another modification for the Bishop's score is the modifiers. Points are added or subtracted according to special circumstances as follows:

One point is added to the total score for:

1. Existence of pre-eclampsia.
2. Each previous vaginal delivery.

One point is subtracted from the total score for:

1. Postdate/post-term pregnancy.
2. Nulliparity (no previous vaginal deliveries).
3. PPROM; preterm premature (prelabour) rupture of membranes .

The higher the Bishop score, the more "ripe" or "favourable" the cervix is for labour induction. A low Bishop score, usually considered less than or equal to 6, is "unripen" or "unfavourable" and will benefit from cervical ripening.[5,6]

BISHOP SCORE=.....(total)			Date of Bishop Score:...../...../.....	
Score	0	1	2	3
Dilation	Closed	1-2	3-4	5
Length	>4	3-4	1-2	0
Consistency	Firm	Medium	Soft	-
Position	Posterior	Midline	Anterior	-
Head: Station	-3	-2	-1,0	+1,+2

CONTRAINDICATIONS FOR IOL

- Prior classic uterine incision or trans fundal uterine surgery.
- Active genital herpes infection.
- Placenta or vasa previa.
- Umbilical cord prolapse.
- Transverse or oblique foetal lie.
- Absolute cephalopelvic disproportion (as in women with pelvic deformities).
- Cervical carcinoma.

SPECIAL CAUTION Required for:

- Previous caesarean section.
- Multiple pregnancy.
- Polyhydramnios.
- Maternal heart disease.
- Severe hypertension.
- IOL is usually not recommended in cases with severe intrauterine growth restriction with oligohydramnios.

RISKS AND COMPLICATIONS OF IOL

- CAESAREAN DELIVERY- especially increased in nulliparous, two-to threefold risks, caesarean rates are inversely related with favourability of the cervix at induction, that is, the Bishop score.
- CHORIOAMNIONITIS- ascending infections.
- UTERINE ATONY- Postpartum atony and haemorrhage are more common in women undergoing induction or augmentation. Intractable atony was the indication for a third of all caesarean hysterectomies.
- UTERINE RUPTURE AND HYPERTSTIMULATION- increased risks of complications, bleeding and caesarean section and other adverse outcomes in patients not properly monitored.
- THICK MECONIUM STAINED LIQOUR.
- ACCIDENTAL RUPTURE OF MEMBRANES & CORD PROLAPSE.
- SYSTEMIC SIDE EFFECTS - Nausea, Vomiting, Diarrhoea, Fever.

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INDICATIONS AND CONTRAINDICATIONS: TIMING OF INDUCTION OF LABOUR

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INTRODUCTION:

The process of artificial stimulation of uterus to start labour is known as induction of labour.1The incidence of induction for various indications has been increased over the past few years. Induction of labour is recommended in all those conditions where the risk of waiting for spontaneous onset of labour is more than the elective delivery. Induction of labour may be associated with increased risk of complications like increased rate of caesarean section, bleeding, hyperstimulation, foetal distress, uterine rupture. So meticulous foetal and maternal monitoring are required.

1. INDICATIONS FOR INDUCTION OF LABOUR

- Preeclampsia ≥ 37 weeks.
- Maternal medical condition refractory to treatment.
- Chorioamnionitis.
- Suspected foetal growth restriction.
- Pre-labour rupture of membranes at term.
- Gestational hypertension ≥ 38 weeks.
- Diabetes mellitus.
- Post-dated pregnancy (>41weeks).
- Uncomplicated twin pregnancy at ≥ 38 weeks.
- Intrauterine growth restriction.
- Oligohydramnios.
- Intrauterine foetal demise.
- Alloimmune disease (at or near term).
- History of intrauterine foetal demise in previous pregnancy (though there is no proven advantage neither in the outcome nor medical, but induction can be offered to alleviate anxiety of the couple).

2. INDUCTION OF LABOUR SHOULD NOT BE ROUTINELY OFFERED IN FOLLOWING SITUATIONS:

- Convenience of patient or care provider when there is no other indication for induction.
- In a non-diabetic women with suspected foetal macrosomia (estimated foetal weight> 4kg)

3. CONTRAINDICATIONS

- Avoid induction of labour when vaginal delivery is contraindicated or is not possible:
- Abnormal foetal lie or presentation (e.g. transverse lie or footling breech).

- Placenta previa or vasa previa.
- Cord presentation.
- History of previous classical or inverted T uterine incision.
- History of uterine surgeries in the past (e.g. myomectomy).
- Pelvis with any structural deformity.
- Invasive carcinoma cervix.
- History of uterine rupture in previous pregnancies.
- Previous pelvic surgeries like VVF/RVF/pelvic floor repair (third/fourth-degree perineal tears), trachelorrhaphy.

4. TIMING OF INDUCTION

4.1 Induction for Pregnancy Beyond Term:[2-6]

Pregnancy at or after 37 weeks to 42 weeks is termed as term pregnancy. Babies born at <37 weeks of gestation have increased incidence of respiratory distress, NICU admissions due to prematurity and underdeveloped organs. Risk of neonatal death is increased significantly in women who continue pregnancy after 41 weeks.

Best time to offer delivery in an uncomplicated pregnancy?

A Cochrane systematic review[5] was done in 2012 to evaluate the benefits versus harm of induction at term or beyond versus waiting for spontaneous onset of labour. Twenty-two randomized control trials involving 9,383 women who were induced at different period of gestations from 37 weeks to over 41 weeks versus those waiting for spontaneous labour till later date were reviewed. Most of the trials adopted the policy to induce at 41 completed weeks. From the review, it was concluded that there are less perinatal deaths (relative risk of 0.31 with 95% confidence interval between 0.12 and 0.88 in 17 trials, 7, 407 women.) in those who were induced than those who adopted expectant management. The difference between adverse outcome in the induction group when compared for the timing of induction (39 to 40 weeks, 41weeks and >41 weeks) was not significant. Hence it was concluded that it is recommended to induce women with uncomplicated pregnancies at or beyond 41 weeks.

The ARRIVE trial,[6] a randomized control trial where 6,000 low-risk nulliparous women were recruited and were induced at 39 weeks and were compared with those who chose for expectant management. There was a decrease in the incidence of caesarean section rate with induction at 39 weeks (18% vs. 22%, relative risk of 0.84 with 95% confidence interval between 0.76 and 0.93).

4.2 Term Prelabour Rupture of Membranes (TPROM):[7-9]

Rupture of membranes prior to the onset of labour in a woman with period of gestation at > 37 completed weeks of gestation is termed as TPROM.

A meta-analysis[8] including 23 trials (8,615 women) done in 2017 compares the risk and benefits of expectant management versus immediate induction in cases of term PROM. The study concluded that there were reduced incidence of maternal infection (chorioamnionitis and endometritis) (relative risk of 0.49 with 95% CI between 0.33 and0.72) as well as definite neonatal sepsis (relative risk of 0.73 with 95% confidence interval between 0.58 and 0.92) in women who has IOL than those who choose to wait for spontaneous onset of labour. The authors noted that most of the inductions were done after 24 hours of membrane rupture.

4.3 Preterm Premature Rupture of Membranes (PPROM): [10,11]

A Cochrane review[10] done in 2017 reviewed 12 RCTs (3,617 women and 3,628 babies) to compare planned early birth versus expectant management for women with PPROM between 24 and 37 weeks and

assess their outcome in terms of feto-maternal wellbeing. From this systematic review, it was concluded that the difference between neonatal sepsis or proven infection with positive blood culture between the early birth and expectant management were not significant with relative risk of 0.93 and 1.24, respectively. However, the incidence of respiratory distress syndrome (relative risk of 1.26 with 95% Confidence interval of 1.05) as well as caesarean section (relative risk of 1.26, 95% confidence interval between 1.11 and1.44,) were more in those with early planned delivery than those with expectant management. The review suggested that the early births (prior to 37 weeks of gestation) were associated with increased risk of neonatal mortality, endometritis, induction of labour and caesarean section. There was reduced risk of chorioamnionitis in women with early birth. It was concluded that in PPROM expectant management with careful observation has better outcome than planned early birth. In the present meta-analysis, there were four trials in which the women were more than 34 weeks of gestation, five trials included women before 34 weeks and two trials included both before and after 34 weeks. When compared it was seen that the incidence of endometritis was decreased in women having early birth in groups after 34 weeks (relative risk of 0.37, 95% confidence interval between 0.10 and 0.40) when compared with the women randomized in trials < 34 weeks (relative risk of 2.23 with 95% confidence interval between 1.29 and 3.84). Incidence of respiratory distress syndrome (RDS) was increased in trials that recruited women greater than 34 weeks gestation (relative risk of 1.45, 95% confidence interval between 1.10 and 1.90, five trials, 2,992 newborns), and a decreased incidence of chorioamnionitis in expectant management in trials that recruited women >34 weeks gestation (relative risk of 0.26 with 95% confidence interval 0.12 to 0.57, three trials, 847 women). This may suggest better infant and maternal outcomes are related when women were managed expectantly after 34 weeks period of gestation. Authors of this review found that there was insufficient evidence to guide the risks versus benefits of immediate birth compared to those who went into spontaneous labour.

In cases of PPROM remote from term it is clear that expectant management with careful observation is the best approach to reduce neonatal complications.

But there remains a dilemma about the management of those who had PROM near term that is after 34 weeks to 36+6 weeks of gestation. As described previously, most of the clinician were of the opinion that there is no benefit of waiting after 34 weeks.

PPROMT trial[11] was done in 2006 to resolve the dilemma whether to go for immediate delivery or wait for spontaneous onset of labour. Here they included 1,839 women, 924 were assigned to the group with immediate delivery and 915 to expectant management. Neonatal outcome was similar in both the groups in terms of APGAR score, neonatal sepsis, pneumonia, circulatory compromise and perinatal or infant mortality. There was a reduction in the incidence of respiratory distress, mechanical ventilation, need for NICU admissions and hospital in the expectant management group. So they were of the opinion that the expectant group has better outcome than the immediate delivery group.

4.4 Diabetes Mellitus

There is only one RCT[12] that compares induction of labour versus expectant management in 200 diabetic women requiring insulin (100 in each group). The result of this study showed that there was a reduction in the macrosomia incidence (birth weight more than 4 kg) in the women who were induced at 38 weeks of gestation than those who waited for spontaneous onset of labour (relative risk of 0.56 with 95% confidence interval between 0.32 and 0.98). The rate of caesarean section was similar in both the groups.

Another Cochrane review[13] done in 2017, included a single trial done on 425 women which compared the pregnancy outcome in women with gestational diabetes who were induced at term to those who received expectant management. No significant difference was seen in the pregnancy outcome in the two groups when compared to rate of caesarean section, maternal mortality or mobility, perineal trauma. No significant difference was seen in the neonatal outcome in terms of macrosomia, shoulder dystocia. Since the number of studies were less, more RCTs are required to make a decision.

4.5 Suspected Foetal Macrosomia

Cochrane review[14] reviewed four trials done on 1,190 which compared the outcome of induction versus expectant management for suspected foetal macrosomia, found no significant difference in the rate of caesarean section, fractures, instrumental delivery, brachial plexus injury, low APGAR score at 5 minutes in both the group. Hence the conclusion was made that elective induction for foetal macrosomia should not be done if there is no other indication for immediate delivery.

4.6 Previous Caesarean Section

A retrospective cohort study done by Stock et al[15] from 1981 to 2007 in the United Kingdom, to see the outcome of elective induction of labour at 39 to 41weeks in women with singleton pregnancies with previous caesarean birth when compared to those who underwent elective repeat caesarean section. The outcome of both the groups was compared to the women who received expectant management. They enrolled 2,960 women in their study. Only 40.1% women needed caesarean section in IOL group. The odds of caesarean section was lower in IOL group than those who were managed expectantly. The risk of neonatal unit admissions was increased. No difference was found in the perinatal mortality in both the study groups (IOL vs. expectant management). However, women who underwent repeat elective caesarean section when compared with the women managed expectantly shows lower risk of perinatal mortality and neonatal admission rates. So the authors were of the opinion that IOL in women with previous caesarean section reduces the chance of repeat caesarean section but increases the risks of neonatal complications.

Another systematic review[16] was published in March 2010, which reviewed 203 papers. The review showed that although rare in both cases but maternal mortality was significantly higher in the group with elective repeat caesarean section (13.4/100,000 women in ERCS vs. 3.8/100,000 in IOL group). Complications like hysterectomy, haemorrhage and transfusions were same in both the groups.

Cochrane review[17] was done in 2017 but they did not find any randomised controlled trial that compares the outcome of women who underwent repeat elective caesarean section versus those who were induced. So no conclusion about the timing of IOL could be made for women with previous caesarean section.

4.7 Breech Presentation

A data published in 2016 by Marcheryet al[18] included 268 women with singleton pregnancies with breech presentation at term. Seventy-three women were induced for various medical or obstetric indications and 195 women were allowed to go into spontaneous labour. It was seen that the rate of caesarean section was higher in the induction group than those with spontaneous onset of labour. There was no increased risk of any adverse perinatal or maternal outcome in the induction group. So the authors concluded that there is no harm if the women with breech pregnancies are induced.

Another retrospective hospital-based study was done between 2003 and 2012 by Burgos J et al,[19] where the babies born after induction for breech vaginal delivery were compared to the babies born to women who went into spontaneous labour. Women with term breech pregnancy (n= 966) were induced and 501 went into spontaneous labour. Study did not show any significant increase in the caesarean section (20.8% vs. 14.8%, P=0.14) rate or poor neonatal outcome. Hence concluding that inducing labour at term is safe and can be offered to those with term breech pregnancies.

In their study, Rojanskyet al[20] also concluded that in the carefully managed cases of breech presentation induction of labour seems to be safe.

4.8 Twin Pregnancy

A Cochrane review[21] done in 2014 reviewed two RCTs done on 271 women with uncomplicated twin pregnancies shows no difference in the women who were induced at 37weeks' gestation and those who were managed expectantly in terms of rate of caesarean section (relative risk of 1.05 with 95% confidence interval between 0.83 and 1.32), perinatal deaths (relative risk 0.34 with 95% confidence interval 0.01 to 8.35) and serious perinatal morbidity (relative risk of 0.29 with 95% confidence interval between 0.06 and

1.38). However induction of labour at 37 weeks decreases the incidence of low-birth weight babies (relative risk of 0.30 with 95% confidence interval between 0.13 and 0.68). Hence the author concluded that inducing a woman with uncomplicated twin pregnancy at 37 weeks does not cause any harm to the baby and mother.

4.9. Hypertensive Disorders in Pregnancy

A Cochrane review[22] published in 2013 reviews 425 women between 24 and 34weeks of gestation included in four randomised control trials. The authors observed that the women who were in interventional group were at increased risk of caesarean deliveries than the expectant management group. Babies were at increased risk of developing hyaline membrane disease, intra-ventricular haemorrhage, more NICU admissions required a ventilator and were admitted in the neonatal units for a longer duration.

Thus the authors were of the opinion that the expectant management should be adopted for those who are remote for term if maternal conditions are stable.

Another multi-centric trial done by Koopmans CM et al[23] enrolled women between the gestational age of 36 weeks and 41 weeks with gestational hypertension and mild pre-eclampsia. A total of 756 women were recruited. Trial showed increased risk of adverse maternal outcome in those who received expectant management when compared to those who were induced (44% vs31%, relative risk of –0.71 with 95% confidence interval -0.59-0.86, P <0.0001). Thus it was concluded that induction of labour should be offered to the women with gestational hypertension and mild pre-eclampsia beyond 37 weeks.

A review[24] published in 2016 revised seven RCTs including 1,501 women with pre-eclampsia to see the effectiveness and safety of elective delivery versus expectant management for the women with pre-eclapmsia and to assess the neonatal outcome before and after 34 weeks. The authors found that in those women who were more than 34 weeks of gestation elective delivery is associated with lower rate complications and need for anti-hypertensive drugs than those managed conservatively (RR-0.64; CI0.51-0.80). Women with elective delivery for severe pre-eclampsia less than 34 weeks of gestation had lesser placental abruption (RR-0.43;CI 0.19-0.98). Babies born to mothers with severe PE less than 34 weeks were at increased risk of intra-ventricular haemorrhage, hypoxic ischemic encephalopathy, and needed ventilatory support.

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METHODS OF CERVICAL RIPENING

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1. INTRODUCTION:

Cervical ripening refers to the softening of the cervix that typically begins prior to the onset of labour contractions and is necessary for cervical dilation and the passage of the foetus. Cervical ripening results from a series of complex biochemical processes that end with rearrangement and realignment of the collagen molecules. The cervix thins, softens, relaxes and dilates in response to uterine contractions, allowing the cervix to easily pass over the presenting foetal part during labour.

In late pregnancy, hyaluronic acid content increases in the cervix. This leads to an increase in water molecules that intercalate among the collagen fibres. The amount of dermatan sulphate decreases, leading to reduced bridging among the collagen fibres and a corresponding decrease in cervical firmness. Chondroitin sulphate also decreases.

Cervical ripening is associated with decreased collagen fibre alignment, decreased collagen fibre strength and diminished tensile strength of the extracellular cervical matrix. An associated change with the cervical ripening process is an increase in cervical decorin (dermatan sulphate proteoglycan 2), leading to collagen fibre separation. Together, these changes lead to softening of the cervix (i.e., ripening).

With uterine contractions, the ripened cervix dilates as the presenting fetal part descends, leading to the reorientation of the tissue fibres in the cervix in the direction of the stress. Under the effect of myometrial contractions, the cervix passively dilates and is pulled over the presenting foetal part. Evidence also indicates that the elastin component of the cervix behaves in a ratchet-like manner so that dilation is maintained following the contraction.

In summary, cervical ripening is the result of the realignment of collagen, degradation of collagen cross-linking due to proteolytic enzymes. Cervical dilation results from these processes plus uterine contractions. This is a complicated series of events in which many changes occur both simultaneously and sequentially. Research in this area is challenging due to both the difficulties inherent in human subjects research and the many differences existing between species.

2. ROLE OF VARIOUS HORMONES IN THE PROCESS OF CERVICAL RIPENING

A complex series of interactions occurs whereby various hormones stimulate the chemical reactions critical for cervical ripening. Associated with cervical ripening is an increase in the enzyme cyclooxygenase-2, leading to a local increase of prostaglandin E2 (PGE2) in the cervix. The increase in local PGE2 leads to a series of important changes associated with cervical ripening, including the following:

Dilation of small vessels in the cervix

Increase in collagen degradation

Increase in hyaluronic acid

Increase in chemotaxis for leukocytes, which causes increased collagen degradation

Increase in stimulation of interleukin (IL)-8 release

Prostaglandin F2-alpha is also involved in the process via its ability to stimulate an increase in glycosaminoglycans.

Cervical ripening is associated with increased activity of matrix metalloproteinases 2 and 9, enzymes that degrade extracellular matrix proteins. Cervical collagenase (also called matrix metalloproteinase 1) and

elastase also increase. Near-term, collagen turnover increases and degradation of newly synthesized collagen increases, leading to decreased collagen content in the cervix.

In animal studies, sex steroids have been demonstrated to be involved in cervical ripening. In the rat cervix, increasing estrogen leads to increased collagenase activity, cervical cell apoptosis and eosinophil infiltration. Animal models also exhibit a decrease in receptor-mediated progesterone activity, but whether this is involved in cervical ripening is unclear.

The role of inflammatory agents in cervical ripening has also been studied. IL-8 can lead to neutrophil chemotaxis, which is associated with collagenase activity and cervical ripening. These inflammatory agents may be particularly important as mediators of cervical ripening associated with preterm labour.

A recent study has focused on the nitric oxide synthase (NOS)/nitric oxide (NO) system. The NOS/NO system has been postulated to have a regulatory role in the myometrium and cervix during pregnancy and parturition. In rat studies, NO and increased NOS activity are associated with uterine quiescence. NOS activity is higher prior to labour and decreases during labour, thereby playing a role in the onset of uterine contractions associated with labour. In rat studies, NO levels and NOS activity behave in an opposite manner in the cervix. Prior to cervical ripening, NOS activity is low and then increases at the time of labour, associated with cervical ripening. NOS activity leading to NO production is the final pathway in inducing chemical changes associated with cervical ripening. In the human cervix, ripening is associated with an increase in induced NOS (iNOS) and brain NOS expression in the cervix.

Resident and migrating inflammatory cells can cause an increase in iNOS activity. Indeed, in the primate, cervical ripening has many aspects of an inflammatory process-tissue remodelling and breakage of chemical bridges between collagen fibres. Inflammatory agents such as IL-1, tumour necrosis factor-alpha and IL-8 seem to be involved in cervical ripening.

NO also appears to play a role in this process because animal studies show that increased cervical NO leads to an increase in metalloproteinase activity, cellular apoptosis in the cervix, and glycosaminoglycan synthesis in the cervix. All of these changes are associated with the cervical ripening process.

NO also could play a role in premature cervical ripening associated with preterm labour, particularly in preterm labour triggered by an infection. Inflammatory cells are rich in iNOS activity, leading to a dramatic increase in NO in the cervix, which stimulates the chemical changes associated with cervical ripening and leads to preterm labour and delivery. Human and animal studies support a role for NO in the process of cervical ripening. NO donors, when applied to the cervix, induce cervical ripening.

To stop preterm labour successfully, both uterine contractions and cervical ripening must be halted. Speculating that this requires blockage of prostaglandin synthesis in the uterine fundus and cervix (and local NO synthesis in the cervix) is tempting. The role that inflammatory agents play in the cervical ripening process could explain the explosive nature of the cervical changes that occur in preterm labour, particularly when associated with uterine infections.

3. EVALUATION OF CERVICAL RIPENING

A variety of techniques have been developed to quantify cervical ripening in order to predict the timing of labour and delivery. This quantification is useful for patients at risk for preterm labour and for helping predict which patients will respond to induction of labour for medical reasons or for postdate pregnancy.

The most commonly used methodology to evaluate cervical ripening is the Bishop score because it is simple and has the most predictive value. This score uses cervical dilation, effacement, consistency, position and the station of the presenting part. Other methods that have been described in the literature, generally for gauging the risk of preterm labour, include ultrasound assessment of the cervix and detection of foetal fibronectin in cervicovaginal secretions.

A Bishop score of 5 or more is considered significant for cervical ripening and favourable for induction of labour. Bishop score is calculated based on cervical position, effacement, dilation, effacement and station of the presenting part, shown in Figures 1 and 2.

FIGURE 1: BISHOP SCORE.

BISHOP SCORE (to assess cervical favorability)

CERVIX	SCORE				BISHOP SCORE MODIFIERS
	0	1	2	3	
POSITION	Posterior	Mid-position	Anterior		**Add1 point for:** • Pre-eclampsia • Each previous vaginal delivery **Subtract 1 point for :** • Postdate pregnancy • Nulliparity (no previous vaginal delivers) • PPROM (premature preterm rupture of memberanes)
CONSISTENCY	Firm	Medium	Soft	>80%	
EFFACEMENT	0 - 30%	30 - 50%	60 - 70%	>5 cm	
DILATION	Closed	1 - 2 cm	3 - 4 cm	+1, +2	
STATION	-3	-2	-1		

FIGURE 2: MODIFIED BISHOP SCORE.

MODIFIED BISHOP'S SCORE (Ease of IOL=ripeness of the cervix)

	SCORE			
	0	1	2	3
Cervical Dilation (cm)	0	1-2	3-4	5-6
Cervical Length (cm)	>4	3-4	1-2	<1
Cervical Consistency	Firm	medium	soft	
Cervical position	Posterior	central	Anterior	
Station (cm in relation to spine)	-3 above spines	-2 above spines	-1 to 0 above spines	Below spines
Total Score 13: Favourable: Score 6-13, Unfavourable Score 0-5.				
Substitue the length of cervix for % of effacement				

A recent study examining over 5,600 nulliparous women undergoing induction of labour found that a simplified Bishop score, including only cervical dilation, effacement, and station, was equally as predictive as the traditional Bishop score in predicting vaginal delivery.[1]

Emerging evidence suggests that ultrasound assessment of the cervix helps distinguish patients at increased risk of preterm labour. In a meta-analysis, Crane and Hutchens evaluated more than 300 studies, including 14 articles involving more than 2,200 women in their final analysis. They found that ultrasound is a strong predictor of preterm birth among asymptomatic women at less than 35 weeks' gestation.[2]

Detection of foetal fibronectin in cervicovaginal secretions has also been used. Foetal fibronectin is a glycoprotein found in amniotic fluid and at the chorionic decidual interface. The absence of this protein in cervicovaginal secretions predicts prolongation of pregnancy. Foetal fibronectin is also predictive of response to prostaglandin application to the cervix at term in order to induce cervical ripening and labour. Currently, evaluation of foetal fibronectin is used predominantly in the assessment and triage of patients for preterm labour.

Bishop scores are somewhat subjective, but a score of less than 5 suggests further ripening is needed, while a score of 9 or greater suggests ripening is completed. No maximum has been determined for the number of doses of a cervical ripening agent that can be given. Indeed, if the patient has no pressing indication for delivery and if foetal well-being parameters are reassuring, the patient can even be discharged, to return in a few days for another attempt at induction. Good clinical judgement is indispensable. A variety of methods have been developed to induce cervical ripening in the preparation of the cervix for labour and delivery.[3]

4.1. Prostaglandins

4.1a. Prostaglandin E2

Two forms of PGE2 (dinoprostone) are available commercially. In randomized trials, the two forms are equivalent in efficacy. The first is Prepidil (in the United States)/Cerviprime (in India), which is formulated as a gel and is placed inside the cervix, but not above the internal os. The application (3 g gel/0.5 mg dinoprostone) can be repeated in 6 hours, not to exceed three doses in 24 hours. The second is Cervidil (in the United States)/Propess (in India), which contains 10 mg of dinoprostone embedded in a mesh and is placed in the posterior fornix of the vagina. This allows for controlled release of dinoprostone over 24 hours, after which it is removed.

Comparison between the use of intravenous oxytocin alone with a combination of oxytocin and either vaginal or intracervical PGE2 demonstrate that prostaglandins result in a significantly lower caesarean delivery rate and an increased proportion of vaginal deliveries within 24 hours. However, patients with ruptured membranes the time of labour induction had an increased rate of chorioamnionitis among those receiving vaginal or intracervical PGE2.[4]

4.1.b. Prostaglandin E1

Prostaglandin E1 analogue (misoprostol) use has been described in a series of articles. This is a synthetic prostaglandin, which is marketed as an antiulcer agent under the trade name Cytotec (in the United States)/Misoprost, Zitotec, Cytolog (in India). One-quarter of a tablet (25 mcg), which can be crushed and placed on the cervix, has been shown in many studies to be quite effective in inducing cervical ripening and labour. The application of the medication can be repeated every 4 hours.

Two meta-analyses comparing randomized trials of vaginal misoprostol with dinoprostone found an increased rate of vaginal delivery within 24 hours and similar caesarean delivery rates in the misoprostol groups and hence conclude that misoprostol is the more effective agent.[5, 6]

Misoprostol has also been administered orally (50–100 mcg, which can be repeated every 4 hours), but the vaginal administration seems to be more efficacious. Vaginally administered misoprostol has been used for cervical ripening and labour induction in pregnancies complicated by oligohydramnios. In these patients, the risk of adverse perinatal outcomes was not increased compared with patients with normal amniotic fluid volumes. Note that the US Food and Drug Administration classify misoprostol (Cytotec) as a pregnancy category X drug. The manufacturer has been ambivalent about this off-label use of the medication, and the Food and Drug Administration only acknowledges that misoprostol is being used in pregnancy.

The American College of Obstetrics and Gynaecology (ACOG) Committee on Obstetrics Practice recommends that misoprostol not be used in the induction of labour after previous caesarean section or major uterine surgery, due to a significant risk of uterine rupture.[7]

The major risk of the above prostaglandin preparations is uterine hyperstimulation. The woman and foetus must be monitored for contractions, foetal well-being, and changes in the cervical Bishop score. Finally, Christensen et al[8] demonstrated that the combination of oxytocin induction, preceded by a dinoprostone insert is safe, and this significantly shortens induction-to-delivery times.

The exception to this appears to be women with previous caesarean deliveries. The ACOG Committee on Obstetric Practice, in its review of pertinent literature, note that the sequential use of prostaglandins and oxytocin appears to increase the risk of uterine rupture in women with a previous caesarean section.[7]

A randomized controlled trial by Al-Ibraheemi et al9that randomized 200 patients into a cervical ripening using misoprostol and a transcervical Foley bulb simultaneously group and a misoprostol alone group reported that the combined group showed shorter time to delivery (15.0 hours vs. 19.0 hours in the misoprostol-only group [P=.001]).

4.2. Low-Dose Oxytocin Infusion

In this method, a low-dose oxytocin infusion is performed, with an increase in dose from 1 to 4 mU/min. Ferguson et al showed this method to be comparable to intravaginal misoprostol for cervical priming.[10] Because of the ease of turning off the oxytocin infusion, this method may have a preferential role in high-risk patients whose foetuses are at increased risk for intolerance of labour.

4.3. Balloon Catheter

A 30-mL to 50-mL Foley catheter filled with saline is effective in inducing cervical ripening and dilation. The catheter is placed in the uterus, and the balloon is filled. Direct pressure is then applied to the lower segment of the uterus and the cervix. This direct pressure causes stress in the lower uterine segment and probably the local production of prostaglandins.

In some studies, the catheter is combined with a saline solution as an extra-amniotic infusion.[11] No evidence suggests that extra-amniotic saline infusion (EASI) increases the risk of chorioamnionitis.[12] A meta-analysis involving 27 studies and 3532 patients found that no difference between Foley balloon and PGE2 use in caesarean delivery rate. This study was hampered by the significant heterogeneity of the studies and subgroup analysis suggested that Foley balloon in combination with oxytocin and EASI may indeed have a higher vaginal delivery rate and a lower rate of tachysystole.[13]

The PROBAAT trial compared the effectiveness and safety of induction of labour using a Foley catheter with induction using vaginal prostaglandin E2 gel. They found that in women with an unfavourable cervix at term, the outcomes were similar, with fewer maternal and neonatal side-effects associated with Foley catheter use.[14]

4.4. Anti-progesterone

Mifepristone (formerly known as RU 486) is an effective anti-progesterone and anti-glucocorticoid that works by binding to progesterone and glucocorticoid receptors. Although individually randomized trials have shown favourable results for its use in inducing labour, a Cochrane Database review concluded that data were insufficient to support its use in labour induction. This review did note a decreased rate of caesarean delivery with mifepristone use, suggesting potential future areas of research.[15]

4.5. Hygroscopic Dilators

Several products are available that can be placed in the cervix and dilated by water absorption. Laminaria is made from dried seaweed. Commercial products (Dilapan and Lamicel available in the United States), are produced from a synthetic hygroscopic material. Several dilators are inserted in the cervix-as many as will fit-and they expand over 12-24 hours as they absorb water. Absorption of water leads to expansion of the dilators and the opening of the cervix. They probably work much the same as the balloon catheter. Women do not need prophylactic antibiotics for the balloon catheter or hygroscopic dilators, unless specific indications exist such as a need for subacute bacterial endocarditis (SBE) prophylaxis.

4.6. Membrane Stripping

Manual separation of the amniotic membranes from the cervix is thought to induce cervical ripening and the onset of labour. The mechanism is unknown, but mechanical disruption of this tissue has been postulated to cause an increase in local prostaglandins by the induction of phospholipase A2 in the cervical and membrane tissues. Such a postulation is certainly consistent with the known stimulation of cervical

ripening by prostaglandins. However, there is no strong evidence at this time that membrane stripping significantly shortens the duration of pregnancy. Authors of a Cochrane Database review on this topic concluded that this practice provides no clinically important benefits.[16]

4.7. Nitric Oxide Donors

Studies are being conducted on the use of nitric oxide donors for cervical ripening with conflicting results. Preliminary small studies evaluating isosorbide mononitrate (40 mg) and glyceryl trinitrate had encouraging results. However, randomized controlled trials comparing misoprostol with and without isosorbide mononitrate have demonstrated contradictory results. Furthermore, a Cochrane Database review of eight studies consisting of 718 patients evaluating the use of nitric oxide donors for cervical ripening in first-trimester surgical abortion found them to be inferior to prostaglandins and associated with more side effects.[17-19]

A randomized, double-blind, placebo-controlled study by Schmitz et al also cast doubt on the use of nitric oxide donors in cervical ripening, finding them to be no more effective than placebo in reducing the rate of caesarean sections in nulliparous women with prolonged pregnancy. The study, of nulliparous women at 41 weeks' gestation, included 678 patients who received vaginal isosorbide mononitrate and 684 women who received a placebo, all on an outpatient basis. The investigators found that the caesarean delivery rate in the isosorbide mononitrate and placebo groups were nearly identical (27.3% vs. 27.2%, respectively) and that side effects occurred more frequently in the women treated with the nitric oxide donor than in the other patients (78.8% vs. 27.9%, respectively).[20]

4.8. Relaxin

Because of the results from a series of animal studies, relaxin has been predicted to have effects on cervical ripening in humans. The findings that porcine relaxin induces cervical ripening in humans supports this conclusion. Paradoxically, human relaxin has no effect on the human cervix, and relaxin is not currently used in cervical ripening or induction of labour. The reason for the species difference is unknown and calls into question the role of human relaxin in human parturition.

In addition, animal research suggests that supplemental hyaluronidase may shorten labour leading to improved induction success.[21] Future research in these areas, and others may lead to improved cervical ripening and labour induction methods.

5. SUMMARY OF INDUCTION OF CERVICAL RIPENING

Induction of cervical ripening is critical to the successful induction of labour in a pregnant patient whose cervix has not gone through the ripening process. Cervical ripening allows the uterine contractions to effectively dilate the cervix. The amount of uterine pressure required to dilate a ripe cervix is thought to be approximately 1,600 mm Hg, while the pressure to dilate an unripe cervix is estimated to be greater than five times that, or 10,000 mm Hg.

6. CONTRAINDICATIONS TO CERVICAL RIPENING

- Contraindications to cervical ripening include, but are not limited to, the following:
- Active herpes.
- Foetal malpresentation.
- Non-reassuring foetal surveillance.
- History of prior traumatic delivery.
- Regular contractions.
- Unexplained vaginal bleeding.
- Placenta previa.
- Vasa previa.
- Prior uterine myomectomy involving the endometrial cavity or classical caesarean delivery.

Previously, a history of a prior low transverse caesarean delivery was considered a contraindication to induction of labour. According to the ACOG Practice Bulletin on Vaginal Birth After Previous Caesarean Delivery (VBAC), induction of labour is not contraindicated in women with a prior low transverse caesarean delivery; however, use of prostaglandins should be avoided in these patients due to a significantly increased risk of uterine rupture.[22] A relative contraindication to cervical ripening is ruptured membranes. At this time, no evidence shows that cervical ripening followed by delayed induction of labour reduces the rate of caesarean delivery.[23]

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CERVICAL RIPENING BY DINOPROSTONE VAGINAL PESSARY

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Induction is the process of initiating contractions in the uterus of a pregnant mother who is not in labour for achieving vaginal delivery. Induction of labour (IOL) is often required in the clinical practice to support natural birth experience.[1]

Induction Methods

The choice of induction mainly depends on the status of the cervix before the IOL. The other important factors considered while selecting a method for induction are unfavourable cervix, nulliparous women and history of a previous cesarean section are associated with a poor chance of successful vaginal delivery.[1]

The mechanical (non-pharmacological) methods used for cervical ripening include digital dilation, use of transcervical Foley catheter, bougies, hygroscopic laminaria tents and amniotomy. Balloon devices and Foley catheter can be used for the mechanical dilatation of the cervix.[2, 3]

Prostaglandin Analogues

The pharmacological options among prostaglandin analogues include prostaglandin E2 (PGE2), PGE1 and PGF2 alpha. The example of PGE2 is dinoprostone. Misoprostol is an example of a synthetic analogue of PGE1.[4]

The risk of systemic side effects with prostaglandins has led to the development of various formulations for local application. These include intra-vaginal tablets or suppositories, intra-cervical or intra-vaginal gels in a single-use syringe, and sustained release intra-vaginal pessary.

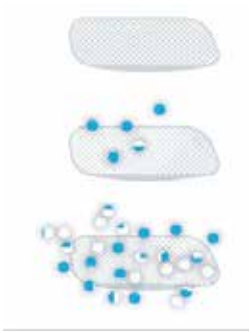
Misoprostol, a synthetic analogue of PGE1, is currently in clinical development in the United States for labour induction. However, this agent has not received approval from major regulatory bodies such as the FDA or EMA. Consequently, the use of misoprostol remains unlicensed in many countries.[5]

A sustained and controlled release of dinoprostone is needed to overcome the potential problems with gel and tablet formulations. The dinoprostone vaginal pessary is an innovative formulation of dinoprostone which is locally inserted. Its novel design provides a controlled release formulation that supplies a continuous low dose of dinoprostone.[6]

Rationale for Development

The dinoprostone vaginal pessary was developed to provide a continuous, controlled release of a low-dose dinoprostone in an easy-to-use formulation. Application and retrieval of the vaginal pessary are simple to perform. Furthermore, the sustained and controlled delivery of a low-dose dinoprostone avoids the administration of doses in excess of the amounts required to bring about cervical ripening and so eliminates the risk of 'dose dumping', which has been associated with an increased likelihood of adverse events. The presence of a retrieval system also means that the pessary can be rapidly and easily removed, immediately eliminating the source of dinoprostone.[9]

Dinoprostone Vaginal Pessary



Dinoprostone Release from the Hydrogel Pessary

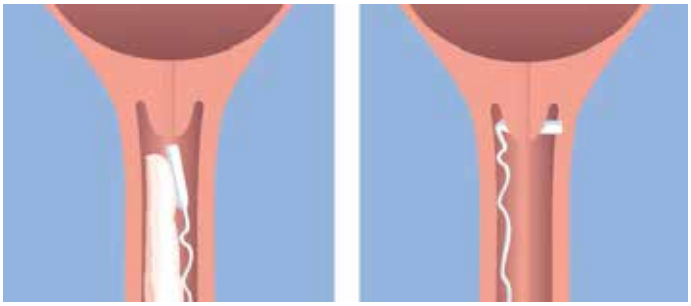
The characteristics of the dinoprostone vaginal pessary compared with dinoprostone gel formulations is summarised in the below table. [10]

Controlled release (0.3 mg/h) dinoprostone vaginal pessary	Intracervical gel (0.5 mg dinoprostone)
Single dose needed	Prepared in single-use syringe system
Provides a controlled and predictable release of dinoprostone (0.3 mg/h over 24 h)	Administration requires speculum and stirrups
Easy to administer, without the involvement of stirrups, speculum or syringe	Frequently spills out of the cervical cavity
Removal is easy, reliable and quick	Contact with amniotic membranes may initiate labour prior to cervical ripening
Slow release and ease of removal confer precise control over the degree of cervical ripening	Repeated dose may be needed
Can be inserted by clinician or trained obstetric personnel	Difficult to remove quickly, requiring irrigation and/ or wiping
Ambulation permitted 20–30 minutes after insertion	
Highly acceptable both to patients and healthcare professional	
Has the capacity to function as cervical ripener and labour inducer	

Administration and Removal

The introduction of the dinoprostone pessary into the vagina and the subsequent removal of the pessary are simple procedures that do not involve the use of a syringe, a vaginal speculum or stirrups.[11] The pessary should remain sealed in the foil package and stored in a freezer (−10 to −25°C) until needed. After opening, it is then held between the index and middle fingers and is positioned transversely, high in the posterior fornix, using only small amounts of water-soluble lubricants to aid insertion.

Administration



Removal

After the pessary (vaginal delivery system) has been inserted, the withdrawal tape may be cut with scissors always ensuring there is sufficient tape outside the vagina to allow removal. Patients should remain recumbent for 20–30 minutes to allow the pessary to hydrate and swell, but after this period they may be ambulatory.10 The vaginal pessary has proved to be highly acceptable to patients while in situ, producing no discomfort in 97% of cases.[13] When removal is required, this can be accomplished quickly and easily through the application of gentle traction to the retrieval tape. An interval of at least 30 minutes is required before the sequential use of oxytocin for the IOL, if necessary, following the removal of the pessary. On withdrawal, the vaginal pessary will have swollen to approximately twice its original size and be pliable.

Contraindications

The dinoprostone vaginal pessary should not be used or left in place under the following circumstances:[10]

- When oxytocic drugs are being administered (the uterotonic activity of oxytocin is potentiated by dinoprostone) suspicion or evidence of foetal distress, a history of difficult or traumatic deliveries, in those with more than three previous full-term deliveries and in those with previous surgery or rupture of the cervix.
- When there is current, or a history of, pelvic inflammatory disease, unless adequate prior treatment has been instituted
- If there is hypersensitivity to PGE2 or any of its excipients
- Previous surgery or rupture of the cervix
- Placenta praevia or unexplained vaginal bleeding in the current pregnancy

Storage

Dinoprostone vaginal pessary should be stored in a freezer (at −10° to −25°C) for a maximum of 3 years.[10]

Efficacy of Controlled-Release Dinoprostone

Placebo-Controlled Trials

Three randomized, double-blind, clinical trials have assessed the efficacy of controlled-release dinoprostone versus placebo in 485 women at term (referred to as studies 1, 2 and 3, respectively).[11,12,13] A subsequent meta-analysis including these trials and other studies comparing dinoprostone with different cervical ripening agents was performed by Crane and Bennett.[12]

The three placebo-controlled trials were similar with respect to design. Inclusion criteria were a singleton pregnancy >37 weeks duration, cephalic presentation, Bishop score <4 at admission, medical or obstetric reason for induction, and <3 previous viable deliveries. Exclusion criteria included previous uterine scar, vaginal bleeding, ruptured membranes, FHR abnormalities, and medical conditions precluding dinoprostone administration. The primary outcome measure for these trials was cervical ripening with treatment success defined as vaginal delivery within 12 h, or a Bishop score >6, or an increase from baseline in Bishop score >3 at 12 h. A number of secondary outcomes were also measured including time to vaginal delivery, time to onset of labour, need for oxytocin (reflecting induction failure) and caesarean section rate. The baseline characteristics were similar in each trial and did not differ between placebo and active-treatment groups, with the exception that in study[3], the mean age of women in the multiparous group receiving placebo was significantly higher than for those receiving active treatment (28.2±5.1 vs. 25.6±5.3 years; P=0.03).[15] In all three trials, the most frequent indication for labour induction was post-term pregnancy.

Dinoprostone was significantly better than placebo for all primary outcomes, and in general, the results were unchanged when nulliparous women were analysed separately. However in study[3], the response to controlled-release dinoprostone in nulliparous women was primarily a cervical change (Bishop score was improved but there were no vaginal deliveries in either placebo recipients or dinoprostone recipients), whereas in multiparous women the response was mainly higher rates of delivery within 12 h.[16] Furthermore, in both nulliparous and multiparous women, the time to onset of labour and to vaginal delivery was significantly shorter in those women receiving controlled-release dinoprostone.[11–13]

The meta-analysis of these three trials confirmed that controlled-release dinoprostone was associated with a significantly higher rate of cervical ripening (OR 3.99 [95% CI 2.71–5.86]; P= 0.0001), onset of labour (OR 18.32 [95% CI 9.49–35.38]; P = 0.0001), and overall treatment success (OR 4.93 [95% CI 3.36–7.24]; P= 0.0001) compared to placebo. Controlled-release dinoprostone was also associated with a significantly lower rate of oxytocin use (OR 0.14 [95% CI 0.06–0.32]; P= 0.0001) and a non-significantly lower rate of caesarean delivery. While parity did not affect most of the outcome measures, multiparous women had 50% shorter labours than nulliparous women.[13]

The efficacy of controlled-release dinoprostone was reviewed by Kelly et al.[14] The primary aim of the review was to determine the effects of vaginal prostaglandin E2 for cervical ripening or IOL in comparison with placebo, no treatment, or other vaginal prostaglandins (except misoprostol). This was reflected by an increase in successful vaginal delivery rates within 24 h, no increase in operative delivery rates, and significant improvement in cervical condition within 24–48 h.

Comparative Trials

A number of trials have examined the efficacy of controlled-release dinoprostone compared with vaginal or intra-cervical gel formulations of dinoprostone, and the prostaglandin E1 analogue, misoprostol.

Three prospective trials and one retrospective study have assessed the comparative efficacy of controlled-release dinoprostone and vaginal or intra-cervical gel dinoprostone.[15–17] The aggregated data from the two prospective trials were also analysed in the Crane and Bennett meta-analysis.[12] In one trial, 73 women who had an indication for IOL for a variety of reasons were randomised to receive either intra-cervical gel (n=36) or a controlled-release (n=37) dinoprostone pessary.[15] Although changes in Bishop scores were similar in the two groups, the mean times to cervical ripening, active labour and delivery were significantly shorter with the use of controlled-release dinoprostone. Hospital stay was also shorter with the controlled-release formulations than with the gel; 3.7 versus 4.4 days, respectively (P=0.03). If active labour had not already begun, oxytocin infusion was initiated 6 h after the final dose of gel or 30 min after removal of the pessary. Oxytocin was administered in 97% of patients receiving dinoprostone gel and in only 76% of patients receiving the controlled-release dinoprostone pessary (P=0.014).[16]

In a previous study, this figure was even less for the dinoprostone pessary group whereby 54% of patients required labour to be initiated or augmented with oxytocin.[17] At least 50% of women required three doses of the gel to achieve full cervical ripening.

In a retrospective analysis of 100 subjects, the time for application to delivery in women who received controlled-release dinoprostone (n=50) was significantly shorter than in those who received intra-cervical dinoprostone gel (n=50) (29.8±22.0 h vs. 62.0±78.8 h, respectively) (P=0.039). In addition, controlled-release dinoprostone was associated with a higher rate of cervical ripening and a higher rate of deliveries within 24 h than dinoprostone gel (80% vs. 56% and 62% vs. 28%, respectively).

Controlled-Release Dinoprostone pessary versus Foleys Catheter for Labour Induction

The meta-analysis of five randomised controlled trials comprising 1,227 women treated with either dinoprostone vaginal pessary (n=612) or Foleys catheter balloon (n=615) that evaluated time from induction to delivery. A subset of a larger meta-analysis of six randomised, controlled trials comprising 1,453 women treated with either dinoprostone vaginal pessary (n=731) or Foleys catheter balloon (n=722).

The Outcome measures were

- Primary: Caesarean section rate, vaginal delivery within 24 h and time from induction to delivery
- Secondary: Maternal parameters and neonatal outcomes
  The results were dinoprostone vaginal pessary versus Foleys catheter:
- Time from induction to delivery was significantly shorter in dinoprostone vaginal pessary group compared to Foleys catheter group (mean difference = 5.73 h; 95% CI: 1.26–10.20; P=0.01).

Efficiency of Dinoprostone Pessary for Cervical Ripening and IOL in Women of Full-Term Pregnancy Compared with Dinoprostone Gel

A meta-analysis of 15 RCTs (n =1,779) evaluated the efficiency of dinoprostone vaginal pessary (n=845) compared with intravaginal or intracervical PGE_2 gel (n=857) for cervical ripening and IOL in women at term

Sub-analysis of seven trials (n =746) compared the efficiency of dinoprostone vaginal pessary (n=377) and intravaginal or intracervical PGE_2 gel (n=369) with respect to vaginal delivery within 24 h.

The women were ≥37 weeks of gestation, with intact membranes and a Bishop score of <7.

Outcomes

- Primary: Rates of vaginal delivery and Caesarean section
- Secondary: Vaginal delivery within 24 h, artificial-assisted vaginal delivery, as well as reasons for caesarean section (e.g. foetal distress, abnormal labour and failure of induction)

Results

- Dinoprostone vaginal pessary vs PGE_2 gel: Vaginal delivery rate within 24 h (seven studies with this outcome)
- Dinoprostone vaginal pessary significantly improved rate of vaginal delivery within 24 h compared with PGE_2 gel (OR 2.35, 95% CI 1.34–4.13; P=0.003)

Safety of Controlled-Release Dinoprostone

The most significant adverse effect of any method of labour induction is uterine hyperstimulation. Compared with placebo, controlled-release dinoprostone increased the rate of hyperstimulation in all three clinical trials. The incidence of uterine hyperstimulation ranged from 5% to 16% in patients treated with controlled-release dinoprostone pessary, but in the trial with the highest incidence the pessary was left in situ after the onset of labour (in error—the dinoprostone pessary should be removed at the onset of labour) and this would explain these higher rates (75% of cases occurred after the onset of labour with dinoprostone pessary still in place). In all three trials, uterine hyperstimulation resolved within 15 min after the removal of the insert. Foetal distress or FHR abnormalities were observed in 3–10% of dinoprostone-recipients, but these also resolved immediately after the removal of the dinoprostone pessary. Rates of uterine hypertonus with FHR changes were similar in controlled-release dinoprostone to rates with other prostaglandin E2 products (OR 1.19 [CI 0.58–2.54]), but misoprostol-induced higher rates of this adverse effect compared with controlled-release dinoprostone (OR 1.53 [CI 1.05–2.22]). Furthermore, there are no safety issues associated with leaving the pessary for longer than 12 h and up to 24 h.[19]

Conclusions

No pharmacological agent has shown consistent benefit over other agents or formulations in clinical trials when both safety and efficacy are considered. However, unlike other agents such as misoprostol, dinoprostone has been licensed specifically for use in cervical ripening and has therefore been subjected to rigorous trials. Irrespective of whether or not an agent is licensed for use in pregnancy, the cost, ease of use, and the patient preference may be the deciding factors when choosing an agent for IOL.

Patient acceptability of controlled-release dinoprostone is excellent and the potential to use this formulation in an outpatient setting may make it more acceptable to women and therefore superior to other agents. In addition, the administration method of controlled-release dinoprostone minimizes the risk of uterine hyperstimulation in comparison to intravaginal or intracervical gels as the pessary can quickly be removed when labour starts or at the onset of any adverse events. The efficacy and safety of controlled-release dinoprostone in an outpatient setting make the product an appropriate choice for cervical ripening.

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NON-PHARMACOLOGICAL METHODS OF INDUCTION OF LABOUR

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1. INTRODUCTION

Induction of labour is a commonly employed procedure in obstetrics. It is defined as an artificial initiation of labour before its spontaneous onset to deliver the foetus. The aim of induction is to achieve a successful vaginal delivery, which is as natural as possible. Various non-pharmacological methods as well as pharmacological agents can be used for induction of labour.

Non-pharmacological methods were used for a very long time to initiate labour. Various herbal beverages like red raspberry leaf tea, black cohosh tea have been used in certain communities. They are thought to stimulate uterine contractions; however, scientific evidence is lacking. Vaginal administration of evening primrose oil, oral administration of castor oil, hot baths, enema have been used with limited efficacy and varied response for induction of labour. There are very few studies to support the use of these measures for induction of labour.[1] Sexual intercourse also leads to release of prostaglandins thus stimulating labour. Nipple stimulation, acupuncture, membrane sweeping and stretching, amniotomy, mechanical dilators like laminar tents and Foley catheter all have been used as non-pharmacological methods for induction of labour.

2. CURRENTLY USED METHODS

2.1 Mechanical Dilators

Hygroscopic dilators and Foley catheter work on the principle of mechanical dilating the cervix by the release of PGF2α by decidua and adjoining membranes and PGE1 by cervix. As per NICE guidelines, mechanical dilatation is not a preferred method of induction of labour. 2 When compared, mechanical dilators used in unfavourable cervix do not result in increased incidence of vaginal birth or reduced caesarean rate.[2] It, however, offers a distinct advantage of minimal side effects, low risk of tachysystole and low cost with ease of storage. Since these dilators do not lead to uterine hyperstimulation, they are commonly used in women with a previous caesarean section. At the same time, the procedure involves a small risk of introducing infection as these methods are introduced vaginally. They may also lead to maternal discomfort and bleeding in low-lying placenta, though rarely.

Cochrane review published in 2012 included 71 RCT including 9,722 women and said that there is no difference in the number of women not delivered within 24 hours or caesarean rates in mechanical methods as compared with prostaglandins with minimal risk of hyperstimulation with foetal heart changes. However the proportion of multiparous women who did not achieve vaginal delivery within 24 hours was higher when compared to multiparous women who received vaginal prostaglandins.[3]

2.1.a. Foley Catheter

Size 18 F Foley's catheter is inserted into cervical os with the help of ring forceps and inflated with saline. The balloon is then pulled and traction given to facilitate stretching of internal os. The Foley catheter is left in situ for 12–24 h. Extra amniotic saline infusion may also be carried out through the Foley catheter in which saline is infused gradually through os but it is generally not advocated.A Cochrane review of 71 studies showed that the use of mechanical dilators had similar efficacy of vaginal delivery with similar caesarean section rates and minimal uterine hyperstimulation as compared to prostaglandins[3]. Recently an open-label RCT was carried out in India comparing the efficacy of Foley catheter and intravaginal misoprostol in hypertensive women. The study concluded that intravaginal misoprostol was more effective in induction of labour with similar incidence of hyperstimulation.[4] Double-balloon catheters have also been tried but there is no distinct advantage over a single-balloon one. With the advent of prostaglandins and widespread use of oxytocin, the use of non-pharmacological methods is limited. Its distinct advantage of lesserincidence of uterine hyperstimulation and foetal distress as compared to prostaglandins favours its use. Non-pharmacological methods especially Foley catheter has been widely studied and evidence points towards similar efficacy to misoprostol. In developing nations, Foley catheters are relatively cheaper and easy to store, hence their use is very common. Currently the use of non-pharmacological methods for induction of labour remains very popular.

2.1.b Hygroscopic Dilators

Like naturally occurring laminaria tent (derived from seaweed) and synthetic osmotic dilator are used by inserting in cervical canal. Due to their hydrophilic property, they act by absorbing water over 12–24 h and increase in size thereby dilating the cervical canal. Laminaria tents are not used commonly at present.

2.2 Amniotomy

Amniotomy involves rupturing of membranes through the cervix to drain the amniotic fluid. This process releases prostaglandins that stimulate uterine contractions. The patient is laid in lithotomy position and using all aseptic conditions, a finger is passed through internal os to separate the membranes from decidua. Using amnihook or curved Kocher clamps, the amniotic fluid is drained.Amniotomy offers a dual advantage of facilitating labour induction along with monitoring colour of amniotic fluid to detect any bleeding, meconium and others. Amniotomy in unfavourable cervix is technically difficult, it entails the risk of prolonged labour and increases the risk of ascending infection, hence generally not preferred. If amniotomy is carried out and the head is not engaged, there is a risk of cord prolapse. It is necessary to monitor the fatal heart during and after the procedure to rule out cord accidents.

There is not enough evidence as per Cochrane review in 2000 to suggest amniotomy alone as an efficacious method to induce labour. 5 Therefore, amniotomy by itself is not recommended for induction of labour unless other methods are contraindicated for fear of hyperstimulation.

2.3 Membrane Sweeping and Stretching

This procedure has been used since 18th century. It involves introducing a finger under aseptic conditions in cervix beyond internal os and sweeping through the uterus circumferentially thus searching the membranes from deciding. This releases PGF2α from decide helping initiate uterine contractions. The procedure can be carried out in office setting while performing vaginal examination.

A Cochrane review of 22 studies of 2,797 women showed that membrane stripping at term reduced the rate of formal induction of labour at 41 weeks. The studies showed that women who underwent membrane stripping had reduced duration of pregnancy and reduced frequency of pregnancy continuing beyond 41 weeks as compared to the women who did not undergo membrane stripping. These trails did not report any maternal side effects of the procedure.[6] However, it is not a recommended method for Rh incompatible pregnancy for fear of Rh isoimmunisation.

3. OTHER METHODS

3.1 Nipple Stimulation

Nipple stimulation releases oxytocin and helps in the stimulation of labour. The commonly used protocol involves massage of the base of areola or nipple for at least 10 minutes at regular intervals to initiate labour with limited success.

A Cochrane review showed that there was a significant reduction in the number of women not in labour after 72 hours when compared with those with no intervention (62.7% vs. 93.6%, relative risk (RR) 0.67, 95% confidence interval (CI) 0.60–0.74); however, there was no difference in the rate of caesarean delivery or in number of women not in labour after 72 h when the outcome was compared among women who were allocated to breast stimulation group and those who were given oxytocin infusion. However this method should not be used in women who are at high-risk pregnancies and time is a constraint.[7]

3.2. Acupuncture

Acupuncture that involves insertion of fine needles at specific points has also been used to induce labour.

A Cochrane review in 2017 identified 22 trials with 3456 women. The review stated that acupuncture did not lead to increase vaginal delivery rates or any reduction in caesarean section rates.[8] It increases cervical ripening but did not shorten labour. Existing evidence also suggested that acupuncture does not reduce the need for additional methods to induce labour, it does not reduce the need for epidural analgesia or operative delivery.[9]

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PHARMACOLOGICAL METHODS OF INDUCTION OF LABOUR

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1. INTRODUCTION

Pharmacological methods of labour induction have been used for decades as methods to manage the timing of labour. Unlike mechanical agents, pharmacological agents can be used for both pre-induction cervical ripening and induction of labour.

2. METHODS CURRENTLY BEING USED

2.1. Prostaglandins

Prostaglandins have the dual advantage of increasing uterine smooth muscle contractility and aiding cervical ripening. Common side effects of prostaglandins can be attributed to their action on other tissues that contain prostaglandin receptors. These include transient fall in blood pressure, nausea and vomiting, and fever (Table 1).

2.1.1 Prostaglandin E2, or dinoprostone, is a commonly used agent for labour induction. It effects are twofold, both initiating uterine contractions and softening the cervix. The exact mechanism of action in cervical ripening is unknown but is thought to be partial due to the effect of locally administered dinoprostone causing collagen degradation secondary to the secretion of collagenase. Dinoprostone is available as an intracervical prostaglandin E2 gel (2.5 ml containing 0.5-mg dinoprostone), as a controlled-release hydrogel pessary (10-mg dinoprostone) or as a vaginal suppository/gel.

Evidence shows 1 that both gel and pessary are effective in achieving cervical ripening when compared with placebo but pessary achieves ripening over a shorter period (11.1 h vs. 15.2 h. Although the pessary is more expensive than gel, the time to achieve vaginal delivery is shorter and the oxytocin use is less frequent, so overall pessary may be cost-effective. Prostaglandin E2 is found to be superior to placebo in increasing Bishop Score, reducing induction failures, and lowering rate of caesarean sections. Comparable outcomes are found between the Foleys and Prostaglandin E2 for mean induction time and caesarean section rate. When compared with misoprostol, prostaglandin E2 takes longer to achieve active phase, a longer induction time, and a higher risk for caesarean section.[2,3]

Dose and Usage of Dinoprostone Preparations[4]

One cycle of vaginal PGE2 tablets or gel consist of one dose, followed by a second dose and third dose after 6 h if labour is not established (up to a maximum of three doses in 24 h), while one cycle of vaginal PGE2 controlled release pessary consists of one dose over 24 h. When offering PGE2 for induction of labour, healthcare professionals should inform women about the associated risks of uterine hyperstimulation (1% with gel and 5% with insert). Prostaglandins E2 (cervical and vaginal) should not be used in the setting of vaginal birth after caesarean section due to the increased risk of uterine rupture. Intravaginal prostaglandins E2 are preferred to intracervical prostaglandins E2 because they results in more timely vaginal deliveries. Oxytocin can be started 30 min after the removal of a dinoprostone insert and 6 h after gel. Foetal heart rate and uterine activity should be monitored for 30 min to 2 h after insertion.

Caution in use is needed in women with glaucoma, severe hepatic and renal dysfunction, and asthma.

2.1.2 Misoprostol

Misoprostol is a synthetic PGE1 analogue that has been approved and marketed for the prevention and treatment of gastric ulcers associated with the use of non-steroidal anti-inflammatory drugs. Misoprostol has also been found to be an effective agent for cervical ripening and labour induction, and these off-label

uses have been widely adopted. Prostaglandin preparations other than misoprostol are expensive and may not be a priority for implementation, especially in low- and middle-income countries.[7]

Evidence shows that[8] misoprostol can be considered a safe and effective agent for labour induction with intact membranes and on an inpatient basis. Misoprostol should not be used in the setting of vaginal birth after caesarean section due to the increased risk of uterine rupture. Oxytocin should be started no earlier than 4 h after the last dose of misoprostol.[9-14]

Misoprostol is more effective than PGE2 to achieve vaginal delivery and results in less epidural use but more uterine tachysystole.

The oral and vaginal routes have a similar reduction of CS rates. The oral route needs more oxytocin stimulation but the vaginal route will have more tachysystole. The lower vaginal dose (25 mcg) tends to need more oxytocin stimulation and the higher vaginal dose (≥ 50 mcg) tends to have more uterine tachysystole. All doses of misoprostol can cause uterine tachysystole. Electronic foetal monitoring should be performed for 30 min after administration of misoprostol and for 60 min after any tachysystole.

In a Cochrane review in 2014,[15] oral misoprostol was found to be effective in inducing (starting) labour. It is more effective than placebo, as effective as vaginal misoprostol and results in fewer caesarean sections than vaginal dinoprostone or oxytocin. It concluded that there was still not enough data from randomised controlled trials to determine the best dose to ensure safety.

The network meta-analysis 2016[16,17] found that misoprostol may be the best prostaglandin for labour induction. The titrated low-dose oral solution was the safest in terms of risk of caesarean section, while vaginal misoprostol tablets (≥ 50 mcg) were found to be the most effective in achieving vaginal delivery within 24 h of induction.

Network meta-analysis provided a unique opportunity to rank prostaglandin treatments in a coherent, methodologically robust manner, and allowed comparisons to be made across outcomes, to help guide clinicians and patients to make informed treatment choices.

This network meta-analysis showed that misoprostol is probably superior to dinoprostone (prostaglandin E2) for labour induction. If treatment rankings for vaginal delivery within 24 h and caesarean section were informally combined, oral misoprostol solution <50 mcg would seem the most highly ranked treatment across the two outcomes, followed by high-dose misoprostol vaginal tablets and then low-dose vaginal misoprostol tablets. However, the width of the credible intervals around the posterior median ranks was considerable, and so caution is urged in the interpretation of rankings and the probability that treatments are "best." There is uncertainty around sustained release vaginal misoprostol: there was insufficient evidence to draw conclusions about its relative safety and efficacy compared with vaginal tablets, which have been examined in a larger number of trials and are estimated with greater certainty.

DOSE AND USAGE

Because misoprostol remains unlicensed for the induction of labour, many practitioners prefer to use a licensed product like dinoprostone. If using oral misoprostol, the evidence suggests that the dose should be 20 to 25 mcg in solution. Given that safety is the primary concern, the evidence supports the use of oral regimens over vaginal regimens. This is especially important in situations where the risk of ascending infection is high and the lack of staff means that women cannot be intensely monitored.

Oral misoprostol has been widely discussed as a method of labour induction. It is recommended for this indication by the World Health Organization (WHO), the International Federation of Gynaecology and Obstetrics (FIGO), and the Society of Obstetricians and Gynaecologists of Canada (SOGC). The dose recommended is 25–50mcg every 3–6 h till patient enters active labour or up to a maximum of five doses. A systematic review suggests that 'Oral misoprostol for the induction of labour is safer than vaginal misoprostol and has the lowest rate of caesarean section'. A recently completed UK National Institute of Health Research (NIHR) funded network and cost-effectiveness analysis included 31 induction regimes evaluated in 611 trials with over 100,000 trial participants. Titrated low-dose oral misoprostol was identified as likely to be the most cost-effective method, and also had a favourable safety profile. Sublingual or buccal misoprostol had significantly higher rates of hyperstimulation. 18-23 More research is required into ways of reducing adverse outcomes in high-risk groups (nulliparous women or those with a scarred uterus), potentially using a combination of mechanical and uterotonic methods.

2.2 Oxytocin

Synthetic oxytocin is the most common and proven method of induction of labour. A network meta-analysis (2016) for labour-induction method found intravenous (IV) oxytocin plus amniotomy (when prostaglandins are unavailable or contraindicated) to most likely achieve vaginal delivery within 24 h.[17]

Exogenous oxytocin produces periodic uterine contractions first demonstrable in the second trimester of pregnancy. Myometrial responsiveness increases with advancing gestational age until 34 weeks, at which time it levels off until spontaneous labour begins when it increases rapidly. Increase in myometrial sensitivity is due to the increase in myometrial oxytocin receptor-binding sites. Receptor activation triggers signalling events that stimulate contractions, primarily by elevating intracellular calcium. Progress during spontaneous labour is not related to increasing oxytocin concentration, uterine contractions are not associated with changes in plasma oxytocin concentration, and hypocontractile labour does not appear to be the result of a deficit of oxytocin. However, gene variations in the oxytocin receptor appear to be associated with the amount of oxytocin required during induction and the duration of labour. [24-28]

Oxytocin cannot be administered orally because the polypeptide is degraded into small, inactive forms by gastrointestinal enzymes. Thus, it is administered intravenously; its plasma half-life is 3to 6min. Low-dose oxytocin protocols are based on studies showing that approximately 40 min are required for any particular dose of oxytocin to reach a steady-state concentration and maximal uterine contractile response.

Cervical status immediately before oxytocin administration is a key factor associated with the duration of induction and the likelihood of vaginal delivery. The Bishop score is the best available tool for assessing cervical status. There is no universally accepted definition of the favourable or unfavourable cervix. Most obstetricians consider a score ≥6 as favourable and a score ≤3 as unfavourable; scores of 4 or 5 are in a grey zone.

OXYTOCIN DOSE AND USAGE

Intravenous oxytocin alone should not be used for induction of labour. Oxytocin is started at least 6 to 12 h after the final dose of dinoprostone gel, 30 min after the removal of dinoprostone insert and 4 hours after the final misoprostol dose.

Oxytocin is preferably administered intravenously by an infusion pump to allow continuous, precise control of the dose administered. [29,30]

In women with a favourable cervix, administration of oxytocin with early amniotomy rather than amniotomy alone is preferred. Early amniotomy may be performed if the head is well opposed to the cervix and dilatation is less than 4 cm.

In women with an unfavourable cervix, pre-induction cervical ripening increases the likelihood of a successful induction. Both pharmacological and mechanical approaches are reasonable choices unless a patient has a contraindication.

There is no single oxytocin regimen that has been shown to be best A common regimen is to make a solution of 60 units oxytocin in 1000 mL crystalloid (60 mU in one mL) to allow the infusion pump setting (mL/h) to match the dose administered (mU/min), for example, a pump infusion rate of 1 mL/h equals 1 mU/min. A synthetic version of the hormone is given as a starting dose ranging from 1 to 2mU/min. It is increased by 1–6 mU/min every 15–40 min. Protocols are typically established by individual hospitals.[31,32]

Dose titration and maintenance - the optimum dosing regimen for oxytocin administration is controversial and no protocol has been subjected to the scientific scrutiny necessary to demonstrate its superiority in both efficacy and safety over another.[33]

Protocols differ as to initial dose (0.5 to 6 mU/min), the time period between dose increments (10–60 min), and maximum dose (16 to 64 mU/min). In a 2014 systematic review of nine randomized trials of high- versus low-dose oxytocin regimens for induction of labour, high-dose oxytocin reduced the induction to delivery interval in high-quality trials but did not decrease the frequency of caesarean delivery compared with low-dose therapy. High-dose regimens were associated with a higher rate of tachysystole than low-dose regimens, but maternal and perinatal complication rates were similar for both regimens. [32]

In both, low - and high-dose protocols, the dose is typically increased until labour progress is normal or uterine activity reaches 200 to 250 Montevideo units (i.e., the peak strength of contractions in mmHg measured by an internal monitor multiplied by their frequency per 10 min). Although there is no evidence-based optimal upper limit for the oxytocin dose, most protocols will limit the oxytocin infusion during labour with a live foetus in the third trimester to not> 40 mU/minute. [32]

Uterine and foetal heart rate monitoring — When uterotonic drugs (prostaglandins, oxytocin) are administered, continuous monitoring of uterine activity and foetal heart rate (FHR) are important so that the dose can be adjusted based on uterine activity and the FHR pattern.

Clinical indications (e.g., FHR abnormalities, tachysystole) should lead to the stopping/reduction in oxytocin until they resolve. However, there is no consensus whether the oxytocin infusion should be maintained or can be lowered/discontinued when the desired labour pattern and progress has been achieved.

In a systematic review and meta-analysis of randomized trials comparing discontinuation of oxytocin when the active phase was reached with continuation until delivery (nine trials, 1538 singleton cephalic term pregnancies), discontinuation resulted in lower rates of caesarean delivery (9.3 vs. 14.7%; relative risk [RR] 0.64, 95% CI 0.48–0.87) and tachysystole (6.2 vs. 13.1%; RR 0.53, 95% CI 0.33–0.84). Discontinuation increased the duration of the active phase (mean difference 28 min 95% CI 4–51 min), but the duration of the second stage was similar in both groups. Approximately 30% of women had oxytocin restarted because of arrest of labour. These results are provocative but limited by small sample size, heterogeneity of oxytocin administration regimes, missing data on common safety measures, and differences in clinical definitions, for example, most but not all trials defined the active phase as ≥5 cm cervical dilation. Based on these findings, it is reasonable for clinicians to either continue or reduce/discontinue oxytocin during the active phase until evidence for best practice emerges. [33–38]

Some investigators have described the pulsatile administration of IV oxytocin at 6- to 10-minintervals as it theoretically simulates normal labour. However, pulsatile administration does not improve outcomes such as caesarean delivery rate, and the induction-delivery time. Pulsatile oxytocin administration requires special equipment and is rarely used in contemporary obstetric practice. There is no maximum cumulative dose limit for oxytocin that is known to improve outcomes.

Tolerance: Most units recommend not discontinuing oxytocin. Oxytocin-induced desensitization of the oxytocin receptor has been demonstrated in vitro, but the clinical relevance of this finding in women who receive prolonged oxytocin stimulation is unknown. Although it has been hypothesised that stopping oxytocin if labour is not progressing and then restarting several hours later will improve myometrial contractility, no clinical evidence supports this theory.

Side effects [39-47]

- Tachysystole (>5 contractions in 10 min, averaged over a 30-min window).
- Hyponatremia – Oxytocin resembles in structure to vasopressin (antidiuretic hormone). If higher doses (> 50 milliunits/min) in large quantities (> 3 L) of hypotonic solutions (e.g., 5%dextrose in water) for prolonged periods of time (≥7 h), excessive water retention can occur and result in severe, symptomatic hyponatremia. This risk may be as high as 5% when the aforementioned conditions are met. Excessive oral intake of hypotonic liquids can have the same effect.

Symptoms include headache, anorexia, nausea, vomiting, abdominal pain, lethargy, drowsiness, unconsciousness, grand mal type seizures, and potentially irreversible neurologic injury. If water intoxication occurs, oxytocin and any hypotonic solution should be stopped. Correction of hyponatremia must be performed carefully by restricting water intake and careful administration of hypertonic saline if the patient is symptomatic.

- Hypotension – Hypotension and tachycardia can result from rapid IV bolus injection of oxytocin. In a randomized trial of 75 women undergoing caesarean delivery and assigned to one of five doses of oxytocin after delivery, the prevalence of hypotension 1min after bolus injection of 5 units of 47% oxytocin.

There are no reports of hypotension with contemporary IV oxytocin doses for induction or labour. However, it is best to administer oxytocin by an infusion pump to control the rate of infusion, avoid adverse cardiovascular effects (arrhythmia, myocardial infarction, hypotension), as well as tachysystole, nausea, vomiting, headache, and flushing.

- Risk of autism – There is no consistent evidence from well-designed studies that oxytocin administration is associated with autism spectrum disorder or any other long-term adverse outcomes for the offspring.

Nonstandard approaches - There is a paucity of data regarding the safety and/or efficacy of glucocorticoids, castor oil, hyaluronidase, isosorbide mononitrate, acupuncture, evening primrose oil, herbal preparations, breast stimulation, or sexual intercourse for labour induction, and none of these can be recommended as an evidence-based approach to labour induction.

2.3. Nitric Oxide (NO) Donors

Recently, this compound has been studied in its use as a cervical ripening agent in term pregnancies undergoing an induction of labour.NO donors may be a useful tool in labour induction. Common side effects with the use of NO donors for cervical ripening include maternal headache and palpitations. In all studies, isosorbide mononitrate was given as a 40–80 mg vaginal dose. There is conflicting data on the efficacy of NO donors in cervical ripening and labour induction.

2.4. Progesterone Receptor Antagonists (Mifepristone)

Mifepristone is a steroidal anti-progesterone and anti-glucocorticoid synthetic drug. In the presence of progesterone, mifepristone acts as a competitive receptor antagonist. Progesterone receptor antagonists may be useful in the induction of labour, acting as a synthetic method to a progesterone withdrawal. Mifepristone should not be used in patients with haemorrhagic disorders or patients who are on long-term corticosteroid therapy. At present, mifepristone is offered as a method of induction of labour to women with intrauterine foetal death.

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TABLE 1.PROSTAGLANDINS

DRUG	ACTION	INDICATION	CONTRA INDICATIONS	DOSE AND METHOD	STORAGE	ADVERSE EFFECTS	ADVANTAGES	DIS ADVANTAGES	STATUS IN INDIA & EVIDENCE
Misoprostol (PG E1) as 25mcg, 100 mcg and 200mcg (scored) tablets for oral and vaginal use	Cervical ripening & Myometrial contractions	Induction of labour; (off label use)- poor bishop (<6, specially <3) and intact membranes	Pregnancy, ectopic pregnancy, active labour suspicion or evidence of foetal compromise prior to induction uterine scar; uterine abnormality; placenta praevia or unexplained vaginal bleeding Foetalmalpresentation; signs/symptoms of chorioamnionitis, pre-existing Cardiovascular disease Concurrent use of oxytocics drugs or other labour induction agents (till further evidence)	Oral/vaginal: 25-50 mcg 4-6 hourly up to 5 doses or active labour (4/6cm) latest evidence: oral dose safer, sustains action and almost vaginal deliveries in 24 hours with less side effects. Oral low dose 20-25 mcg solution titrated @every 2 hours is most safe and cost effective latest recommendation.	Room tempratur e below 25°C	Diarrhoea, abdominal pain, fever dyspepsia, flatulence, nausea and vomiting; headache	Currently rated Best inducing, agent if cervix is unfavourable, Low cost, easy availability & storage, good for low middle income resources,	Specific contrain dications/ more tachysystole, FHR changes and uterine rupture a.c.t other methods. Require intense maternal & fetal monitoring through out	Approved for Off-Label use for evidence refer to text (Misoprostol)
Dinoprostone (PGE2) as intracervical gel (0.5 mg in 2.5ml), vaginal gel (1mg, 2mg), vaginal pessary/ insert 10mg, PGE2 tablet (0.5mg)	Cervical softening agent causing collagen degradation, initiate uterine contractions	Cervical ripening and Induction of labour in poor bishop score (<6), with /without PROM	Hypersensitivity, Glaucoma, severe renal, hepatic dysfunction, asthma, active labour, when vaginal delivery is contraindicated, previous caesarean, non-vertex presentation, prolonged ROM (relative CI)	Cervical Gel: 0.5 mg single dose syringe intracervical application 2–3 times @ 6-12 hourly in 24 h (bring gel to room temperature, insert in endocervix, patient to lie supine for 30 minutes, monitor uterine activity & FHR for 30 minutes, start oxytocin 6 hours after last dose) Vaginal gel: 2-5 mg, 2-3 applications @6h apart (bring gel to room temperature, insert in posterior fornix, patient to lie supine for 30 min, monitor uterine activity and FHR for 30 minutes,	Cervical & vaginal Gel: 2-8°C Vaginal pessary/ insert: -20-10°C	Hypersensitivity, Nausea, vomiting, hyperstimulation (1–5%), FHR changes (1%) rarely uterine rupture	More effective than placebo, comparable to mechanical methods in efficacy, more safe but less efficacious than misoprostol. Vaginal insert has slow and predictable release and precise control of cervical ripening, single application and easy insertion and removal.	Storage and temperature maintenance, Gels require positioning, stirrups, repeated applications, are difficult to irrigate if hypersitimulation occurs, have unpredictable release and action.	Approved in India. Intracervical Gel, Vaginal pessary are available in India For evidence refer Dinoprston e above

DRUG	ACTION	INDICATION	CONTRA INDICATIONS	DOSE AND METHOD	STORAGE	ADVERSE EFFECTS	ADVANTAGES	DIS ADVANTAGES	STATUS IN INDIA & EVIDENCE
				start oxytocin 6 h after last dose) Vaginal pessary/insert: once in 24 hours (insert frozen pessary after removal from pack into posterior fornix in transverse position, recumbent position for 2 hours, oxytocin to be started 30 minutes after pessary removal.)					
Oxytocin (synthetic) 5 iu/ml 5 iu/0.5 ml 10iu/ml	Action through myometrial oxytocin receptor binding & activation	Induction of labour when cervix is favourable (Bishop &>6), in cases where prostaglandins are contraindicated or unavailable can be used for IOL in unfavourable cervix also Augmentation of labour, following prostaglandins for maintenance of labour	Medically indicated IOL (Same as above) + prolonged use is not recommend ed for severe preeclampsi a, CV disorder and severe anemia	Intravenous solution , use infusion pump **Low dose protocol:** Initial dose:1-2 mU/min Increase @ 1-2 miu at 30 min. interval Usual dose reqd. 8-12 mU/min Max dose before reassessment - 30 mU/min High dose: Initial dose: .4 to 6 mU/min Increase @ 4-6miu at 15 to 30 min. interval Usual dose reqd. for labour: 8 to 12 mU/min Maximum dose before reassessment -30 mU/min	Store at 2-8 degree C	Tachysys tole FHR changes, hyponatr emia & water intoxication, rarely convulsions, uterine rupture, hypersen sitivity, neonatal jaundice, retinal haemorrh age, low Apgar? autism, PPH, nausea & vomiting, cardiac arrhythmia	Easy availability, low cost is best method when cervix is favourable, can be used as an alternative when prostaglan din is not available or contraindic ated		

MONITORING IN INDUCTION OF LABOUR

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Monitoring by definition is supervising or checking the quality of a procedure or process over time. Induction of labour (IOL) may increase the need for operative interference hence not only monitoring labour, but it is also required to monitor the indication and method of induction.

Prerequisites Prior to Induction

1. REVIEWING THE INDICATION OF IOL

The main goal of IOL is to achieve vaginal delivery within 24 h and reduce the rate of caesarean delivery without increasing adverse maternal and neonatal outcomes. During the antenatal period, it is important to counsel the patient regarding the following issues and documented:

- Conditions when induction will be offered
- When, where and how IOL will be carried out
- Possible duration of induction
- Support and pain relief
- Alternative options to IOL
- Risks and benefits of IOL in specific circumstances and methods
- Success rate of IOL and later options

2. PREINDUCTION ASSESSMENT

At the time of induction:

- Reconfirm the period of gestation using reliable clinical history and early scans
- Determining foetal presentation
- Estimating foetal weight
- Performing a cervical examination to decide whether a cervical ripening agent is indicated
- Cardiotocograph for foetal well-being

3. DECIDING THE METHOD OF INDUCTION

The method of induction largely depends on the Bishop score.

Cervical ripening would be required for women with unfavourable cervix (Bishops score less than or equal to 6). In women with favourable cervix, labour can be induced with oxytocin without the need for a ripening agent.

Cervical Ripening

Evidence for Use of Cervical Ripening Agents

Outcomes using Dinopristone PGE2

As compared to placebo or no treatment, studies have shown a reduced likelihood of vaginal delivery not achieved in 24 h, a reduced rate of continuation of unfavourable cervix after 12–24 ha reduced need for oxytocin augmentation with the use of dinoprostone. There was no difference in the risk of caesarean delivery between vaginal PGE2 and placebo in the subgroup of women with unfavourable cervices.[1]

Outcomes using Misoprostol PGE1

Compared to no treatment or placebo, there was no significant difference in vaginal deliveries not achieved within 24 h and caesarean deliveries. When compared with other vaginal prostaglandins for the outcome of vaginal deliveries within 24 h women receiving misoprostol were more likely to deliver within 24 h and were less likely to require oxytocin augmentation.[2] Compared with oxytocin, vaginal misoprostol increased the likelihood of participants delivering vaginally within 24 h and lesser chances of instrumental deliveries.2 Compared to balloon catheters, misoprostol did not have a statistically significant difference in the likelihood of vaginal delivery within 24 h, or difference in caesarean delivery rates.[3]

Outcomes using Oxytocin- In general, the use of oxytocin is less successful when used in women with a low Bishop score, and as such, a ripening process should be used prior to administering oxytocin to women with unfavourable cervixes.

There was no difference in the likelihood of caesarean deliveries among women receiving misoprostol or women receiving vaginal PGE2, cervical PGE2 or oxytocin.[4]

Monitoring of Labour Following Induction

Monitoring Following Cervical Ripening with Prostaglandins

Bishop score should be reassessed 6 h after vaginal PGE_2 tablet or gel insertion, or 24 h after vaginal PGE_2 controlled release pessary insertion, to monitor the progress of labour.

Monitoring Following Induction with Oxytocin

Oxytocin is typically given intravenously by low-dose and high-dose protocols, preferably given through infusion pumps. The target is to achieve strong contractions every 2–3 min, or a uterine activity of 200–250 Montevideo units. There is no benefit in increasing the dose when one of these endpoints is achieved. Clinical features like FHR abnormalities or tachysystole should lead to the reduction in oxytocin until they resolve.

However, there is no consensus about whether the oxytocin infusion routinely should be maintained or can be lowered/discontinued when a desirable labour pattern and progress has been achieved. In a systematic review and meta-analysis of randomised trials comparing discontinuation of oxytocin when the active phase was reached with continuation until delivery (nine trials, n= 1538 singleton cephalic term pregnancies), discontinuation resulted in lower rates of caesarean delivery (9.3 vs. 14.7%; relative risk [RR] 0.64, 95% CI 0.48–0.87) and tachysystole (6.2 vs. 13.1%; RR 0.53, 95% CI 0.33-0.84) . Discontinuation increased the duration of the active phase (mean difference 28 minutes, 95% CI 4–51 min), but the duration of the second stage was similar in both groups. Approximately 30% of women had oxytocin restarted because of arrest of labour. These results are provocative but limited by small sample size, heterogeneity of oxytocin administration regimes, missing data on common safety measures, and differences in clinical definitions (e.g., most but not all trials defined the active phase as ≥5 cm cervical dilation.[5]

Monitoring Foetal Heart

Continuous CTG monitoring of labours that are induced is preferable.

If CTG is not available, intermittent FHR monitoring (every 15 min in the first stage of labour and every 5 min in the second stage) is recommended.

It is important to watch for pathological CTG changes, vaginal bleeding, rupture of membranes, uterine hyperstimulation, adverse maternal reactions like severe nausea and vomiting, fever and chills.

Monitoring for Complications of IOL

Induced labours should have strict maternal and foetal monitoring protocols. The general physical condition and the intensity and frequency of uterine contractions should be monitored to diagnose conditions like uterine tachysystole, electrolyte imbalance or even uterine rupture.

The interpretations and management of abnormal foetal heart rate patterns are vital to the optimal outcome of labour.

Foetal Heart Rate Monitoring

Cardiotocography (CTG) is an integral part of intrapartum care in most high-income countries. However, one of its limitations is the varied interobserver agreement in interpretation-.Various guidelines follow different criteria in interpreting CTG. These guidelines have important differences, not only in the definition of individual CTG features but also in the criteria used for overall tracing classification. Though there is agreement in defining baseline heart rate, accelerations and variability, there is disagreement about defining decelerations in all the three criteria.[6]

Three-tiered classification systems usually suggest no action for category I/normal tracings and rapid intervention for category III/pathological tracings. Hence, a low percentage of tracings considered normal may be associated with a higher rate of obstetric intervention, whereas a low percentage of tracings considered pathological may be associated with poor neonatal outcomes. Category II/ suspicious includes a broad spectrum of heterogeneous FHR patterns that are inconsistently associated with foetal acidemia, making clinical management of these situations more uncertain. In a study in 2016 by Santo et al, it was found that ACOG group classified 81% of tracings as category II, whereas the suspicious classification was only selected by 52% in the FIGO group and 33% in the NICE group.[6]

Foetal Heart rate patterns

Category I-Normal (a CTG where all of the following four reassuring features are present)

- Baseline rate: 110–160 bpm
- Variability: ≥5 bpm
- No decelerations
- Accelerations: present

Category II/Suspicious- Any one of the following

- Bradycardia (<110 bpm) or Tachycardia (>160 bpm)
- Baseline variability - Minimal variability - Absent variability with no recurrent decelerations - Marked variability
- No accelerations - Absence of induced accelerations after foetal stimulation
- Variable decelerations with other characteristics such as slow return to baseline, overshoots or shoulders
- Periodic or episodic decelerations - Recurrent variable decelerations or recurrent late decelerations accompanied by minimal or moderate baseline variability
- Prolonged deceleration

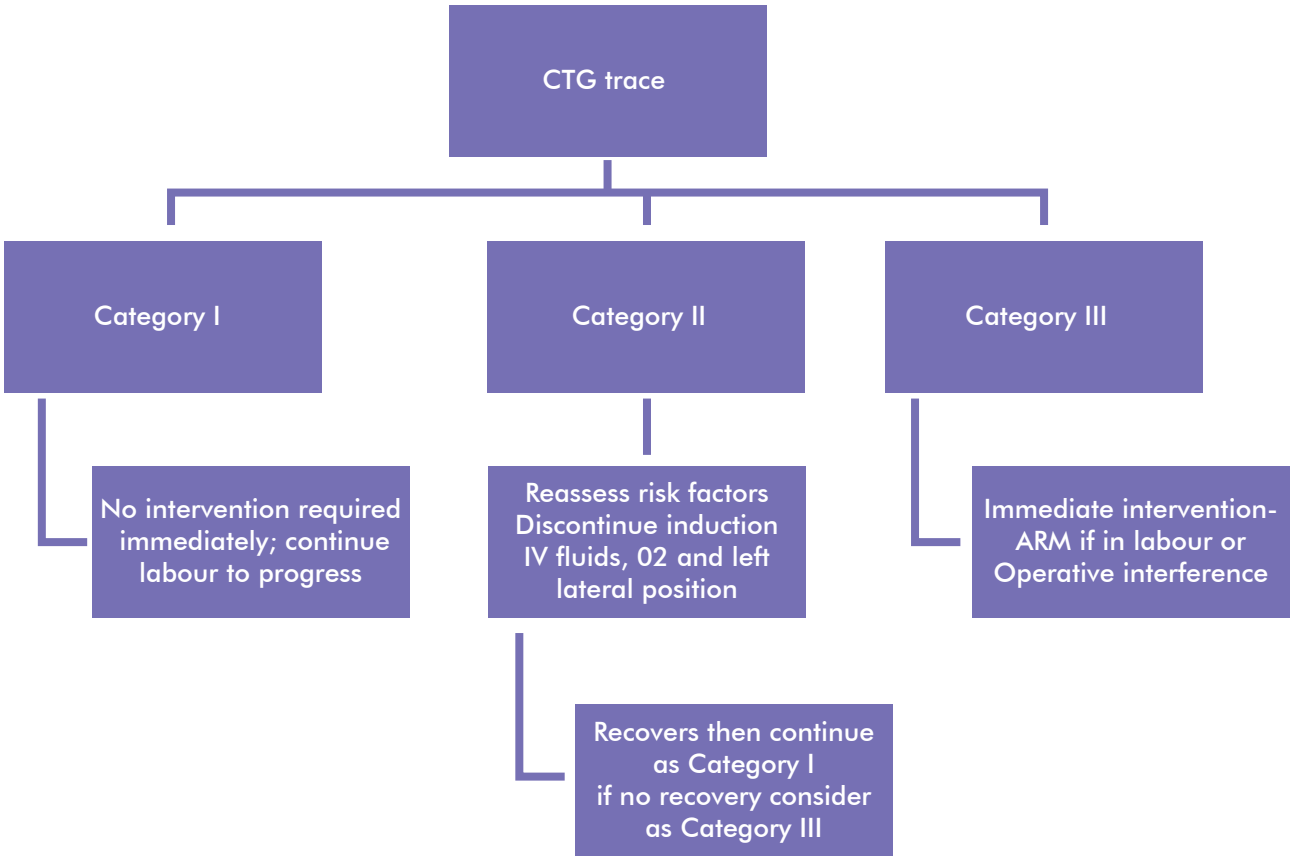
Category III/ Pathological- Any one of the following

- Baseline rate -<100 bpm or > 180 bpm
- Sinusoidal pattern ≥ 10 min
- Absent baseline FHR variability and any of the following: - Recurrent late decelerations/Recurrent variable decelerations

Intervention based on the above classification

- Several studies have shown that CTG has a high sensitivity and a limited specificity in the prediction of foetal hypoxia/acidosis.[7–10]

The following flowchart is suggested for intervention based on the category of the trace



Labour progress : The average duration of the latent phase of labour is longer in induced labour. In two observational studies, the total length of time from admission to delivery in women who were induced was 3 to 4 h longer than in those who were expectantly managed (regardless of cervical status).Once women who have been induced enter active labour (cervical dilation 6 cm), progression appears to be comparable to progression in women with spontaneous active labour. The duration of the second stage is similar in induced and spontaneous labours.[11]

Failed Induction

There has not been a strong consensus regarding the standard for defining a failed induction. The term can be used specifically for caesareans that are performed because the latent phase has continued for an extended length of time and, in the clinician's assessment, it is unlikely that the active phase will be reached or that vaginal delivery will be achieved.[12]

The term is not used for inductions in which an operative intervention is performed to treat active phase protraction or arrest, prolonged second stage, non-reassuring foetal status, or a maternal indication for prompt delivery. Latent phase of labour of cervical ripening is excluded from diagnosing failed induction. [13]

The definition for PGs is "failure to induce progressive labour after one cycle of treatment", consisting of the insertion of two vaginal PGE2 tablets (3 mg) or gel (1–2 mg) at 6-h intervals or one PGE2 controlled released pessary (10 mg) over 24 h.[14]

Conclusions:

1. Monitoring of induced labour starts with reviewing the indication, method and monitoring during labour
2. There was no difference in the likelihood of caesarean deliveries among women receiving misoprostol or women receiving vaginal PGE2, cervical PGE2 or oxytocin
3. Reassess Bishop's score 6 h after vaginal PGE2 tablet and gel and 24 h after vaginal PGE2 pessary

4. Continuous CTG monitoring is ideal for induced labour, if not available intermittent foetal heart monitoring is recommended along with monitoring of foetal and maternal complications
5. CTG has inter-observer and intra-observer variation and clinical management is more uncertain in Category II traces
6. Although the duration of latent phase is longer, the duration of active and second stage are comparable in induced and spontaneous labour

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PAIN RELIEF DURING INDUCTION OF LABOUR

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1. INTRODUCTION

Labour analgesia is known from the days of ether and chloroform in 1847 which has now given way to the practice of evidence-based labour pain management. Newer techniques like combined spinal epidurals and low-dose epidurals facilitate ambulation. Usage of remifentanil for patient-controlled intravenous analgesia, the introduction of newer local anaesthetics and adjuvants has dawned a new era in labour analgesia.

2. PAIN THRESHOLD IN INDUCED LABOURS

Induced labours, in general, more painful as compared to spontaneous labours. This is evident by many trials conducted worldwide. One cohort study in Italy compared the effects of spontaneous (n = 31) and prostaglandin-induced labour (n = 30) on the minimum analgesic dose (MAD) of epidural sufentanil in the first stage of labour in women (at or after 37 weeks of gestation with cervical dilation 2–4 cm) requesting epidural pain relief in labour. The initial dose was sufentanil 25 μg and analgesic effectiveness was assessed using 100-mm visual analogue scale (VAS) pain scores. The MAD of sufentanil in spontaneous labour was 22.2 μg (95% CI 19.6 to 22.8 μg) and 27.3 mcg (95% CI 23.8 to 30.9 micrograms) in induced labour, and the latter was significantly greater than that of spontaneous labour (P = 0.0014) by a factor of 1.3 (95% CI 1.1 to 1.5). This suggests that prostaglandin induction of labour produces a greater analgesic requirement than spontaneous labour.1

3. EFFECTS OF EPIDURAL ANALGESIA ON INDUCED LABOUR

One RCT[1] and one cohort study were identified relating to analgesic requirements in induced and spontaneous labour. There were no significant differences in the duration of labour, modes of birth or foetal outcomes.

Two RCTs[1] compared early and late epidural. There was no significant difference between the two groups in achieving full dilation, vaginal birth rate, caesarean section rate or instrumental delivery rate and APGAR scores at birth. Women in the early epidural group had lower pain scores, better quality analgesia and higher satisfaction, but they were more likely to experience transient hypotension. Hence it was concluded that there is no benefit in waiting for cervical dilatation to give epidural.

A similar systematic review2 of vaginal prostaglandins and oxytocin relating to epidural requirement was done which suggested that a significantly higher epidural usage was associated with induction of labour with intravenous oxytocin than with vaginal PGE2 (RR 1.11; 95% CI 1.04 to 1.19, nine RCTs) in women with different parity, cervical and membranes status[2].

It can be inferred from the evidence that induced labours require labour analgesia. Labour analgesia neither affects the mode or time of delivery nor does it have any adverse effect on neonatal outcome.

Which is the ideal analgesia in labour? What does evidence say?

Although progress is being made for an ideal labour analgesia effective for longer periods, no studies were identified for satisfactory analgesia available to women who are progressing rapidly in labour.

4. METHODS OF PAIN RELIEF IN LABOUR ANALGESIA

4.1. Non-Pharmacological Agents

Water bath, support during labour and acupuncture may be beneficial for the management of pain during labour. There has been no proven scientific data analysis of the quality of pain relief offered by these techniques due to a small number of subjects studied.[3]

4.2. Pharmacological Agents

Pethidine (meperidine), an opioid agonist, is the most frequently used opioid worldwide. Sosa et al3 have concluded that pethidine should not be administered in labour for inadequate dilatation of the cervix as there is no benefit and that there is an increased risk of neonatal adverse outcome.

Intravenous ketamine is also not safe in labour as a patient often requires anaesthetic dosages that may compromise the airway.

Fentanyl is a highly lipid-soluble synthetic opioid with analgesic potency 100 times that of morphine and 800 times that of pethidine. Its onset of action after intravenous route is rapid within 2–3 min with short duration of action and no major metabolites, makes it superior for labour analgesia. It can be administered in boluses of 25–50 μg every hour or as a continuous infusion of 0.25 μg/kg/h and can be administered by patient-controlled intravenous analgesia (PCA).4,5

Tramadol is a pethidine-like synthetic opioid with potency 10% that of morphine. It has no clinically significant respiratory depression at usual doses of 1–2 mg/kg body weight. The onset of action is within 10 min of intramuscular administration and the duration lasts for approximately 2–3 h.

Remifentanil is an ultra-short acting synthetic potent opioid. It has a rapid onset of action and is readily metabolized to an inactive metabolite. The effective analgesia half-life is 6 min thus allowing effective analgesia for consecutive uterine contractions. The recommended dose of remifentanil is an intravenous bolus of 20 μg, with a lockout interval of 3 min on the PCA pump. Maternal monitoring during intravenous PCA with remifentanil should be one to one as maternal hypoventilation is more common and there are more episodes of oxygen saturation falling to <94% on pulse oximetry.[5]

4.2.a. Inhalational Analgesia

Nitrous oxide (Entonox), which is administered as 50:50 mixtures of oxygen and nitrous oxide for short duration. Inform the woman that it may make her feel nauseous and lightheaded.[4,5]

4.2.b Regional Analgesia

Central neuraxial analgesia is the gold standard technique for pain control in obstetrics that is currently available.

Techniques used- The techniques that are available are Epidural analgesia, Combined Spinal Epidural analgesia (CSEA), Patient controlled epidural analgesia (PCEA)

Dosage- Presently all labour epidurals are low-dose epidurals. Traditionally, a high concentration (0.2–0.25%) of local anaesthetic has been used to maintain labour epidural analgesia. In the last decade, the concentration of local anaesthetic used to maintain labour epidural analgesia has been decreasing (0.0625–0.125%) with a reduced total dose of local anaesthetic and lesser side-effects, such as motor blockade.[6]

Maintenance of intrapartum analgesia is either performed by intermittent manual boluses or through patient-controlled or continuous epidural infusion pumps.[6]

Controversies with Epidural Analgesia
Increased Rate of Operative and Instrumental Delivery

The Cochrane Database Systemic trials have emphasized that epidural analgesia had no statistically significant impact on the risk of caesarean section.[6,7]

COMET study states that there was a 25% decrease in instrumental deliveries with the use of labour analgesia.[7]

When to Offer Analgesia in Labour?

The ACOG and the American Society of Anaesthesiologists (ASA) have also jointly emphasized that there is no need to wait arbitrarily till the cervical dilation has reached 4–5 cm and endorsed a statement that "Maternal request is a sufficient indication for pain relief in labour." [8]

Precautions in Labour

Passive descent should be encouraged along with delayed and monitored pushing during birth to safely increase spontaneous vaginal births and decrease instrumental deliveries. This was highlighted by the Pushing Early or Pushing Late with Epidural (PEOPLE) Study conducted in the United Kingdom.[9,10]

There is a controversy regarding discontinuation of epidural analgesia late in labour to improve a woman's ability to push. But there was no significant reduction in instrumental deliveries in early and late discontinuation of epidurals as studied in various RCT's.[11]

Epidural and Vaginal Birth After Caesarean Section

ASA and the Society of Obstetric Anaesthesiologists and Perinatologists (SOAP) recommend early placement of neuraxial analgesia to patients attempting vaginal birth after previous caesarean delivery.[5]

Side Effects with Epidural Analgesia

In two recent randomized trials, there were no significant differences in the incidence of long-term back pain between women who received epidural pain relief and women who received other forms of pain relief.[11]

Practice points

If a woman is contemplating regional analgesia, talk with her about the risks and benefits and the implications for her labour, including the arrangements.

It has to be explained to the patient that

- It provides more effective pain relief than opioids.
- It is not associated with a long-term backache.
- It is not associated with a longer first stage of labour or an increased chance of a caesarean birth.
- It may be associated with a longer second stage of labour.
- It will be accompanied by a more intensive level of monitoring and intravenous access, and so mobility may be reduced.[3]

Care and observations for women with regional analgesia

- Always secure intravenous access before starting regional analgesia. Preloading not required.
- During the establishment of regional analgesia or after further boluses (10 ml or more of low-dose solutions), measure blood pressure every 5 min for 15 min.
- If the woman is not pain-free in 30 minutes after each administration of the local anaesthetic/opioid solution, recall the anaesthetist.
- Assess the level of the sensory block hourly.
- Encourage women with regional analgesia to move and adopt whatever upright positions they find comfortable throughout labour.
- Delay pushing for at least 1 h after full dilatation to allow descent and longer if the woman wishes, after which actively encourage her to push during contractions
- Birth should occur within 4 h regardless of parity.
- Do not routinely use oxytocin in the second stage of labour for women with regional analgesia.
- Foetal heart monitoring using cardiotocography should be done for at least half an hour during administration of regional analgesia and after each further bolus.
- Regional analgesia can be continued until after completion of the third stage of labour and for episiotomy repair.

CONCLUSION:

- There is evidence that women in whom labour is induced have greater analgesia requirements than those with spontaneous onset of labour.
- Oxytocin-induced labours may have greater analgesia requirements than those induced with vaginal prostaglandins.
- Women need the pain relief appropriate to them which can range from simple analgesia to epidural analgesia.
- Labour analgesia does not negatively affect the mode of delivery and, obviously, improves maternal satisfaction.
- Early compared with late administration of epidural analgesia does not prolong labour or increase the need for assisted birth in women whose labours were induced, but is associated with greater maternal satisfaction.
- Epidural or combined spinal–epidural analgesia can be used for establishing regional analgesia in labour. Either patient-controlled epidural analgesia or intermittent bolus are the preferred modes of administration for maintenance of analgesia.
- Use of ultrasound guidance and micro-catheters offer the potential to overcome difficulties of placement in difficult cases.

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COMPLICATIONS AND THEIR MANAGEMENT DURING INDUCTION OF LABOUR

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INTRODUCTION:

Induction of labour is associated with certain complications. Meticulous monitoring of labour that is induced is, therefore, necessary to avoid or early detection of these complications so that timely interventions can be done. Uterine hyperstimulation, failed induction, cord prolapse, uterine rupture, sepsis, precipitate labour, postpartum haemorrhage and maternal death are some of the complications.

COMPLICATIONS:

Uterine hyper-contractility (hyperstimulation or tachysystole): Uterine hyperstimulation is one of the most common complications of induction of labour. The incidence of uterine hyperstimulation with or without foetal heart rate changes varies between 1 and 5%.[1] There are varied definitions given by ACOG for uterine hyperstimulation. Uterine hyperstimulation (tachysystole) may occur with or without FHR changes and is defined as:

- Four or more contractions in 10 min over a 30-min period [2] or
- Contractions lasting more than 2 min in duration [3] or
- Contractions of normal duration occurring within 60 s of each other[4]

In the presence of abnormal FHR patterns and uterine hypercontractility, tocolysis should be considered with 0.25 mg subcutaneous terbutalin.[5] Caution should be taken while using betamimetics in patients with cardiac disease. In case of suspicious or non-reassuring cardiotocograph secondary to oxytocics, their administration should be discontinued. In cases of suspected or confirmed acute foetal compromise, delivery should be accomplished as soon as possible. (appendix 1: chart)

Failed induction: Failed induction is defined as failure to establish labour after one cycle of treatment, consisting of the insertion of two vaginal PGE2 tablets (3 mg) or gel (1–2 mg) at 6-h intervals, or one PGE2 controlled released pessary (10 mg) over 24 h. In the presence of unfavourable cervix, the incidence of failed induction is estimated to be 15%.[6] If induction fails, decisions about further management should be made in accordance with the woman's wishes and should take into account the clinical circumstances.

The subsequent management options include:

- Further attempt to induce labour (the timing should depend on the clinical situation and the woman's wishes)
- Delivery by caesarean section

CORD PROLAPSE:

Prolapsed cord is always a potential risk at the time of membrane rupture, especially when the membranes are ruptured artificially.

Precautions to reduce cord prolapse that should be observed are:

- Engagement of the presenting part should be assessed before induction
- Umbilical cord presentation during the preliminary vaginal examination should be looked for and avoid dislodging the baby's head.
- Amniotomy should be avoided in the high floating head.

MANAGEMENT:

Cord prolapse if diagnosed before full dilatation:

- Assistance should be immediately called and preparations made for immediate birth in theatre.
- Manual replacement of the prolapsed cord is not recommended.
- To prevent vasospasm, there should be minimal handling of loops of cord lying outside the vagina.
- To prevent cord compression, it is recommended that the presenting part be elevated either manually or by filling the urinary bladder.
- Cord compression can be further reduced by the mother adopting the knee–chest or left lateral position
- Caesarean section is the recommended mode of delivery in cases of cord prolapse when vaginal birth is not imminent in order to prevent hypoxic acidosis.
- Vaginal birth can be attempted at full dilatation if it is anticipated that birth. Would be accomplished quickly and safely, using standard techniques and taking care to avoid impingement of the cord.

UTERINE RUPTURE:

Women with scarred uterus (caesarean delivery, hysterotomy, myomectomy) are prone for uterine dehiscence or rupture. Uterine rupture at the time of induction of labour is an unusual event in an unscarred uterus. Women with previous caesarean section and no vaginal deliveries, induction of labour carries a relatively high risk of uterine rupture/scar dehiscence despite all precautions, including intrauterine pressure monitoring.

Induction in a scarred uterus has to be rationalised and taken with proper precaution. Monitoring with continuous electronic foetal monitor can identify foetal tachycardia or decelerations early that can signal an imminent rupture or a dehiscence. Close monitoring and judicious use of tocolytics is mandatory especially in a scared uterus or a multigravida and a multipara. In cases of clinical suspicion of scarred uterus, an immediate delivery by an emergency caesarean section should be planned.

INFECTIOUS MORBIDITY:

Induction of labour can be associated with puerperal sepsis in small number of cases that are already at risk of infections like women with prolonged rupture of membrane. Premature rupture of membranes (ROM) have shown a higher association of infective morbidity.[7,8] Prolonged duration of ROM needs to be documented and appropriate antimicrobials should be started .

INCREASED RISK OF PRECIPITATE LABOUR AND POSTPARTUM HAEMORRHAGE

Precipitate labour has been noted as a result of prostaglandin especially PGE1 derivative and assessment of uterine response should guide the use of further doses. Atonic postpartum haemorrhage is common and universal practice of active management of third stage of labour is essential. Traumatic postpartum haemorrhage due to bucket handle tears, rotational cervical tears are associated and should be looked for and appropriately managed .

MATERNAL DEATH :

Inadvertent indiscriminate use of oxytocics especially misoprostol can cause amniotic fluid embolism especially in cases of precipitate labour and PROM.

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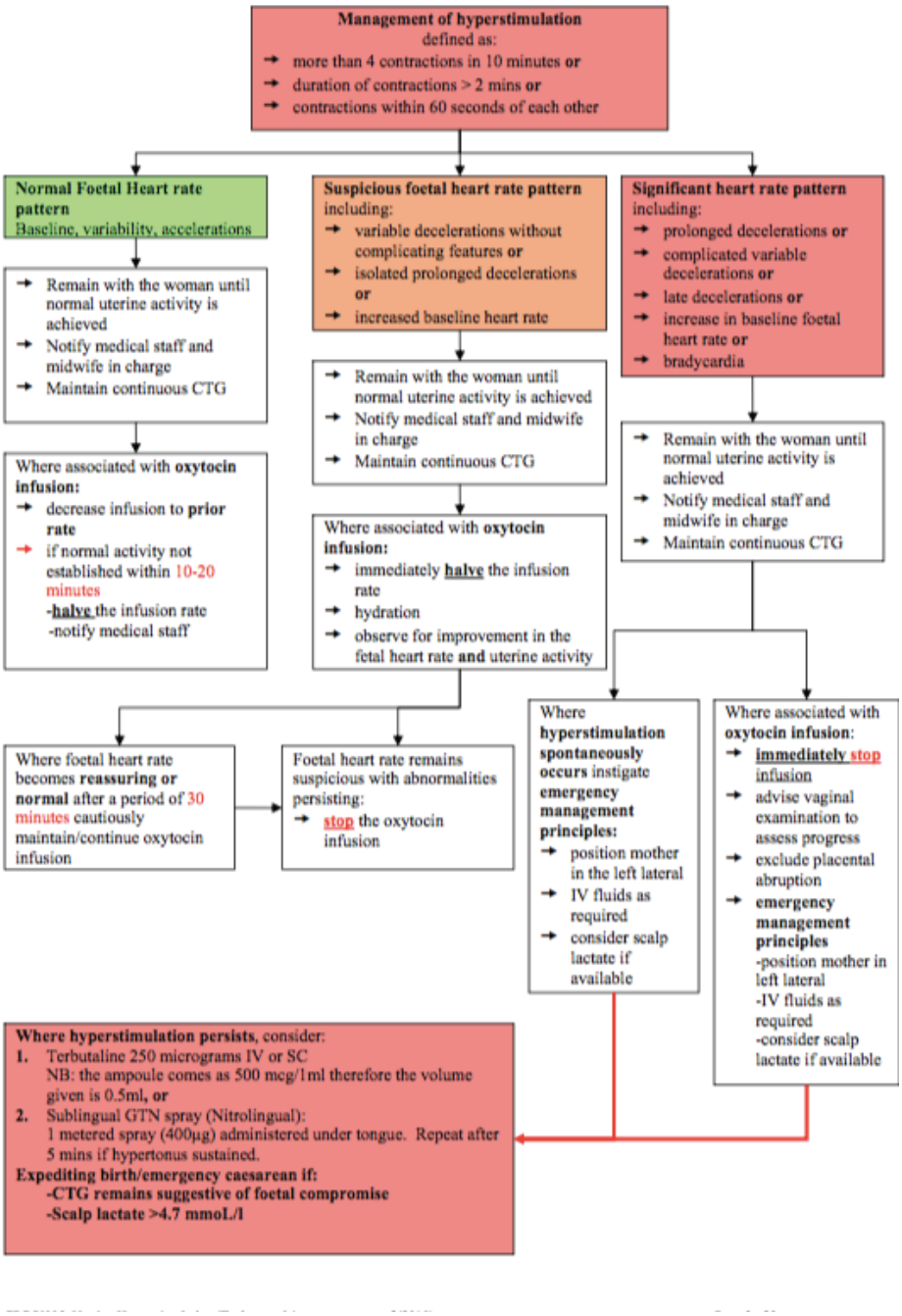
FIGURE 1


Management of hyperstimulation
defined as:
→ more than 4 contractions in 10 minutes or
→ duration of contractions > 2 mins or
→ contractions within 60 seconds of each other
Normal Foetal Heart rate pattern
Baseline, variability, accelerations
→ Remain with the woman until normal uterine activity is achieved
→ Notify medical staff and midwife in charge
→ Maintain continuous CTG
Where associated with oxytocin infusion:
→ decrease infusion to prior rate
→ if normal activity not established within 10-20 minutes
-halve the infusion rate
-notify medical staff
Suspicious foetal heart rate pattern
including:
→ variable decelerations without complicating features or
→ isolated prolonged decelerations or
→ increased baseline heart rate
→ Remain with the woman until normal uterine activity is achieved
→ Notify medical staff and midwife in charge
→ Maintain continuous CTG
Where associated with oxytocin infusion:
→ immediately halve the infusion rate
→ hydration
→ observe for improvement in the fetal heart rate and uterine activity
Where foetal heart rate becomes reassuring or normal after a period of 30 minutes cautiously maintain/continue oxytocin infusion
Foetal heart rate remains suspicious with abnormalities persisting:
→ stop the oxytocin infusion
Significant heart rate pattern
including:
→ prolonged decelerations or
→ complicated variable decelerations or
→ late decelerations or
→ increase in baseline foetal heart rate or
→ bradycardia
→ Remain with the woman until normal uterine activity is achieved
→ Notify medical staff and midwife in charge
→ Maintain continuous CTG
Where hyperstimulation spontaneously occurs instigate emergency management principles:
→ position mother in the left lateral
→ IV fluids as required
→ consider scalp lactate if available
Where associated with oxytocin infusion:
→ immediately stop infusion
→ advise vaginal examination to assess progress
→ exclude placental abruption
→ emergency management principles
-position mother in left lateral
-IV fluids as required
-consider scalp lactate if available
Where hyperstimulation persists, consider:
1. Terbutaline 250 micrograms IV or SC
NB: the ampoule comes as 500 mcg/1ml therefore the volume given is 0.5ml, or
2. Sublingual GTN spray (Nitrolingual):
1 metered spray (400µg) administered under tongue. Repeat after 5 mins if hypertonus sustained.
Expediting birth/emergency caesarean if:
-CTG remains suggestive of foetal compromise
-Scalp lactate >4.7 mmoL/l

INDUCTION OF LABOUR IN SPECIAL SITUATIONS

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1. INTRODUCTION

There are certain conditions where decision for termination of pregnancy, when to terminate and how to induce labour is of concern.[1] These conditions like intrauterine foetal demise (IUFD), Pregnancy with previous caesarean section, prelabour rupture of membranes at term (TPOM), premature prelabour rupture of membranes (PPROM), twin pregnancy and breech presentation are referred as special situations.

2. LABOUR IN SPECIAL SITUATIONS

2.1. Intrauterine Foetal Death

Foetal demise after 24 weeks of gestation is called as intrauterine foetal demise and is estimated to occur in 1% of pregnancies. Diagnosis of IUFD should be confirmed by ultrasound before declaring to the family. Women should be offered a choice of immediate induction of labour or expectant management depending on the wish of women and presence of any other risk factor that warrants an early delivery like abruption, ruptured membranes, preeclampsia, and other. Since 85% of women will go in spontaneous labour within 3weeks[2] expectant management is a reasonable option in the absence of any high-risk factor.[3] If woman choose to delay the delivery for more than 48 h, testing for DIC should be done twice a week. Those who choose to wait should be explained about the risk of coagulopathy and decrease in the value of post-mortem reports due to decomposition of dead foetus.

Prostaglandins are first-line drugs to be used for induction of labour. Mifepristone single dose of 200 mg orally 36–48 h prior to induction is indicated.[4]Misoprostol can be used in preference to PGE2 (off label).Before 28 weeks vaginal misoprostol is the most effective method. For <34 weeks, 100–200 μg 3–6 h sublingually, orally or vaginally (total 1,20μg). For >34 weeks, 50–100μg 3–6 h sublingually, orally or vaginally until birth.[5,6] In > 34 weeks, transcervical catheter and/or oxytocin infusion can be used. In previous caesarean section, discussion of safety and benefits of different methods should be undertaken with the patients. Mifepristone alone can increase the chance of labour within 72 h. Mechanical methods for IOL in IUFD with previous caesarean should be used in clinical trial settings7

2.2. Prelabour Rupture of Membranes at Term

Rupture of membranes at term but prior to onset of labour is termed as term prelabour rupture of membranes (TPROM).[8,9] There is a 8–10% risk of pregnancies having TPROM.[10,11] Whenever a woman comes with the complaint of leaking, first it is vital to confirm the diagnosis. When there is diagnostic uncertainty, sterile speculum examination may be done. Digital vaginal examination should be avoided unless immediate induction is planned. Women with no other indications to expedite delivery and who choose expectant line of treatment should be appropriately offered and supported after informing potential risks and benefits. Theoretically, the risk of infection increases if interval between rupture of membranes and delivery increases. Induction of labour is appropriate approximately 24 h after PROM.[12] Induction of labour with oxytocin is the first option if the cervix is favourable. Active management of term PROM with induction is associated with reduced maternal infective morbidity. In case of unfavourable cervix prostaglandins followed by oxytocin should be used. Antibiotics use is associated with a decreased risk of infection.

2.3. Premature Prelabour Rupture of Membranes (PPROM)

Prelabour rupture of membranes prior to 37 weeks is called PPROM[13,14] which occurs in approximately 3 % of pregnancies.[15] A digital vaginal examination should be avoided where PPROM is suspected. The diagnosis of PPROM is best achieved by maternal history followed by a sterile speculum examination. Ultrasound examination is helpful in some cases to confirm the diagnosis. Antenatal steroids should be administered till 36 weeks of gestational age. Antibiotics should be given for 10 days. Amoxicillin clavulanic acid combination is not recommended due to increased risk of necrotizing enterocolitis.[16]

Management according to the gestational age:

- If 24-34 weeks →Expectant management

  No pervaginal examination, antibiotics, steroids, monitoring for evidence of infection and magnesium sulphate infusion for neuroprotection if delivery happens before 32 weeks.

- If > 34 weeks →Delivery should be considered. Expectant management may be offered after proper counselling about the increased risk of chorioamnionitis and its consequences and decreased risk of serious respiratory symptoms in the neonate and a decreased chance of Caesarean section. Emerging evidence discusses the decreased risk of RDS by prolonging delivery after 34 weeks. Tocolysis is not recommended as it does not significantly improve outcome. It may be given to delay delivery till the effects of steroids occur. Induction with PGs as effective as oxytocin but there are more chances of infection.

2.4. Previous Caesarean Section

With the increasing number of women undergoing a caesarean section, it has become a matter of concern whether to induce women in subsequent pregnancy or wait for spontaneous labour as there are chances of hyperstimulation and scar dehiscence or uterine rupture. Induction of labour remains an option for the women undergoing a planned trial of labour after caesarean section (TOLAC). However proper counselling of woman is a must as the success rate of achieving VBAC decreases in case of previous CS with IOL. There is1.5-fold increased risk of caesarean delivery and three-fold increased risk of uterine rupture with induction of labour. IOL using mechanical methods, that is, Foley's catheter is associated with lower risk of scar rupture compared to induction by prostaglandins Misoprostol is not recommended for IOL in a woman with previous LSCS.

A UK study of registry data of women with a previous caesarean section who underwent induction of labour with prostaglandins (n = 130) reported spontaneous vaginal birth in 50% of cases, with 11% requiring instrumental birth and 39% requiring caesarean sections. There were no cases of uterine rupture.[17]

A cohort study from caesarean birth registry data in the United States compared the risks associated with attempting a vaginal birth in women with previous caesarean section (n = 17,898) with the risks in those women with elective caesarean section without labour (n = 15,801). There were 48 uterine ruptures in women attempting vaginal birth after induction of labour (n = 4,708) compared with 24 in women with spontaneous labour (n = 6,685) (1% vs. 0.4%; OR 2.86, 95% CI 1.75 to 4.67).[18]

2.5. Twins

The optimal timing for birth in a twin pregnancy is uncertain with clinical support for both elective delivery at 37 weeks or expectant management till spontaneous labour.

A Cochrane review [19] with two RCTs compared elective delivery at 37 weeks to expectant management. There were no statistically significant differences identified between a policy of elective birth at 37 weeks' gestation and expectant management with regards to birth by caesarean section (two studies; 271 participants; risk ratio (RR) 1.05; 95% confidence interval, elective birth at 37 weeks gestation for women with an uncomplicated twin pregnancy (CI- 0.83 to 1.32); perinatal death or serious perinatal morbidity (two studies; 542 infants; RR 0.34; 95% CI 0.01 to 8.35); or maternal death or serious maternal morbidity (one study; 235 women; RR 0.29; 95% CI 0.06 to 1.38). There were no statistically significant differences identified for the pre-specified secondary maternal and infant review outcomes reported by these two trials between the two treatment policies (including for: haemorrhage requiring blood transfusion; instrumental vaginal birth; meconium-stained liquor; Apgar score less than seven at 5min; admission to neonatal intensive care; birth weight less than 2,500 g; neonatal encephalopathy; and respiratory distress syndrome). While not a pre-specified review outcome, elective birth at 37 weeks, compared with expectant management was shown to significantly reduce the risk of infants being born with a birth weight less than the third centile (one study; 470 infants; RR 0.30; 95% CI 0.13 to 0.68).

Hence the authors concluded that uncomplicated twin pregnancies should be offered induction at 37 weeks as perinatal mortality increases at each additional week after 37 weeks.

2.6. Breech Presentation

Vaginal breech delivery at term is controversial and whether induction of labour should be advised is a debatable topic.

To decrease the breech incidence at term, external cephalic version should be offered and performed. Those with failed ECV or persistent breech decision regarding mode of delivery should be discussed with the family and an informed consent should be taken about the mode of delivery and associated merits and demerits. Caesarean section is the preferred method of delivery. If the patient does not want to undergo ECV or ECV fails and the patient is not willing for caesarean delivery written informed consent should be taken after explaining the risks associated with breech vaginal delivery.

A retrospective review of patient records (n = 641) in Ireland reported that safe breech vaginal birth can be achieved with strict selection of induction of labour in specific circumstances, induction of labour criteria and adherence to a careful intrapartum protocol and with an experienced obstetrician in attendance.[20] Compared with planned vaginal birth, planned caesarean birth reduced perinatal or neonatal death and serious neonatal morbidity (RR 0.33, 95% CI 0.19 to 0.56), at the expense of increased short-term maternal morbidity (RR 1.29, 95% CI 1.03 to 1.61).[21]Hannah's trial although famous, is very old and not applicable to developing countries where there is a role of vaginal breech delivery in parous patients.

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INDUCTION OF LABOUR – AT MATERNAL REQUEST

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1. INTRODUCTION:

Elective induction at maternal request is one that has no medical indication, either maternal or foetal. This issue needs to be addressed as there is a significant increase in induction rates. The rising rates may be the result of more autonomy being offered to women concerning their delivery and may represent convenience for the obstetrician and the pregnant woman. It may also just be apparent due to a decrease in indicated indications when compared to an overall increase in numbers in case of induction of labour.[1]

Some women request elective induction of labour for pragmaticsocial and emotional reasons and to allow advance scheduling ofdomestic matters and the presence of partner during labour and birth, and avoidance of distant journey during labour. TocoPhobia– the fear of labour pain is another condition in which women wants to plan painless labour and delivery at convenient time with availability of all experts, an obstetrician, anaesthetist ,and a neonatologist,not forgetting the birth companion.

2. OVERVIEW OF AVAILABLE DATA

No evidence was identified that assessed the effects of induction of labour at maternal request. However, three RCTs from one systematic review were identified that assessed the effects of elective induction of labour at term 37–40 weeks of gestation in women with no medical reasons.

A systemic review[2] that assessed the effects of induction of labour versus expectant management from 37 to 42 weeks of gestation three RCTs (n=1,300), included women at 37–40 weeks of gestation. Meta-analysis of these three trials found no significant difference in perinatal deaths (RR 0.32 95% CI 0.03 to 3.09 two RCTs) between the induction and expectant management group as there were two deaths in the expectant management group, one from a congenital heart condition and one from cord compression. However, the induction group was significantly less likely to have caesarean birth (RR 0.58, 95% CI 0.34 to 0.99, three RCTs) but more likely to require assisted vaginal birth (RR 1.71, 95 CI 1.23 to 2.39 two RCTs)

Indirect evidence suggested that compared with expectant management, elective induction of labour at 37–40 completed weeks of gestation without medical reasons was associated with a higher incidence of assisted vaginal birth and a lower incidence of caesarean birth.

A study by Revickyet al[3] was done to see the relationship between elective induction of labour and mode of delivery. Totally 11,6660 women were enrolled out of which 8,314 had a vaginal delivery, 1,571 had an emergency caesarean section and 1,775 had instrumental delivery. On further evaluation, it was found that there was a decreased risk of instrumental delivery in women with elective induction of labour and no effect on the rate of caesarean section.

Another study done by Stock et al[4] suggest that there was a decreased incidence of perinatal mortality in the women with elective induction of labour at term than those managed expectantly.

Fisch and colleagues (2009)[5] reported a study done on 653 women, in which there was a reduced rate of the caesarean section following inductions in their institutions by insisting on strict protocols and considering the potential risks associated with elective induction of labour at term. The mandatory prerequisites while offering the option were a detailed counselling of the potential risks and outcome with the women who were for elective induction at maternal request, empowering her to make an informed choice,39 completed weeks of gestations, Bishop Score of 8 in nulliparous and 6 in multiparous women.

3. INTERPRETATION OF EVIDENCE

There is no evidence to determine the effects of induction of labour on maternal request. Evidence on induction of labour at 37–40 completed weeks without a medical indication is limited. This aspect needs more research and evidence, especially in India.

A study was done in French women to see the estimated rate of elective induction on maternal request by Coulm et al[6] it was seen that out of all the inductions done 13.9% were elective induction out of which 47.3% were done on maternal request.

Another study[7] showed that the incidence of Induction of labour for conditions not justified by medical professionals, that is, those done for reasons other than medical indications is 15% and not associated with an increased risk of complication.

3.1. Advantages of Elective Induction8:

- Planning to deliver in the day time when most of the specialists are available.
- Benefits both the mother and the foetus in situations where continuing the pregnancy might pose more problems.

Allows the woman to plan her delivery, a painless delivery with good analgesia instead of opting for caesarean delivery – in cases of Tocophobia but this needs evidence.

3.2. Disadvantages of Elective Induction:

- May increase the risk of CS or operative vaginal deliveries although evidence is not conclusive.
- Might increase perinatal morbidity in the form of foetal distress, birth asphyxia, and increased release of meconium
- Studies show a greater use of epidural analgesia and pain perception in induced labour
- Mobility of the woman may be restricted and some women perceive it as more dissatisfactory than spontaneous labour.

4. RECOMMENDATION ON INDUCTION OF LABOUR AT MATERNAL REQUEST

Induction of labour should not be routinely be offered on maternal request. However, under exceptional circumstances for example this can be considered as if the woman partner is soon to be posted abroad with armed forces induction may be offered at or after 40 weeks.

This can be considered when the woman is not able to reach medical facility easily or not really approachable to the obstetric facility when the husband is in military posted far away, visits infrequently to the family .There should be the individualization of each woman before consideration of her request for elective induction of labour and need more research and evidence to come to a conclusion.

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INDUCTION OF LABOUR: PROCEDURE EDUCATION LITERATURE

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The education material and information to be provided to the patient before induction of labour is being summarised in the following sections.
We recommend that you read this handout carefully in order to prepare yourself or family members for the proposed procedure. In doing so, you will be aware both from benefits and procedure and outcome and safety of the procedure. If you still have any concerns and doubts after reading this we encourage you to clarify your doubts with your doctor.

HEADINGS

1. **Reason for induction**
2. **Gestational age**
3. **Cervical status**
4. **Estimated foetal weight**
5. **Method of induction**
6. **Monitoring**
7. **Pain Relief**
8. **Outcome of induction**
9. **Complications**

1. Reason for Induction

Labour induction is the process by which your doctor will start uterine contractions that may lead to a vaginal birth of your baby. There are several reasons that your doctor would induce your labour. It is done when it is felt that the intrauterine environment is not healthy for your baby. There can be many indications and your doctor would have discussed the indication and the method of induction in your case.

2. Gestational age

Women with uncomplicated pregnancies are usually given opportunity to go into spontaneous labour.But these women are offered induction of labour from 41+0 to 42+0 weeks if they don't go into labour spontaneously to avoid prolonged labour.

If a woman chooses not to have induction of labour, her decision must be respected. Healthcare professionals should discuss her care with her and should be offered increased antenatal monitoring consisting of at least twice weekly cardiotocography and ultrasound estimation of the amniotic fluid index.

3. Cervical Status

The success of labour induction in leading to a vaginal delivery depends on many factors, one of which is how far your cervix is dilated and shortened. The more dilated and the more shortened your cervix, the more likely you are to deliver vaginally. We may give you medicine to ripen your cervix prior to starting uterine contractions.

This process is done in the hospital usually in the labour and delivery unit. This will allow us to monitor your baby prior to the start of the induction to make sure the baby is doing well.

4. Estimated Foetal weight

The approximate weight of your baby with respect to the size of the pelvis has a major bearing on the possibilities of a vaginal delivery. Your doctor will assess the weight clinically or with the help of an ultrasound. Although there are not many contraindications, the weight of the baby above 4kg calls for a more cautious approach to planning the route of delivery.

5. Method of Induction

There are various methods of induction of labour. Drugs like prostaglandin E2 and oxytocin will be offered depending on the condition of your cervix and your background medical and obstetrical (history of previous childbirth). Your doctor will discuss the options, the advantages and side effects of these methods with you.

6. Monitoring

The condition of the mother and baby will be assessed before starting the induction of labour. Following induction you will be monitored in the labour ward and depending on the method used and your response to the inducing agent, further plan would be made regarding the mode of delivery.

In the usual practice, a repeat internal examination is performed after 6 h of prostaglandin E2 instillation. Once the cervix becomes favourable, the labour is augmented by oxytocin followed by a rupture of the bag of membranes at the appropriate time.

The labour is monitored during this time by checking the condition of the mother and the baby, every half an hour.

7. Pain Relief

You can discuss the various options of pain relief available to you with your doctor.

8. Outcome of IOL

A labour induction does not always lead to a vaginal delivery. Sometimes, despite the best efforts of your doctor, a caesarean section may have to be done. The success of the labour induction will depend on the situation in which labour was induced.

Also, a labour induction may lead to an operative delivery such as a forceps delivery or a vacuum delivery.

9. Possible Complications of the Procedure

All procedures, regardless of complexity or time, can be associated with unforeseen problems. They may be immediate or delayed in the presentation. We would like you to have a list so that you may ask questions if you are still concerned. These complications include the following:-

HYPERSTIMULATION

Hyperstimulation usually means that your uterus is having too many contractions in a 10-min period. This can also include evidence that the foetus may not be tolerating the contraction pattern. The rate of hyperstimulation with PGE2 gel is approximately 1% if placed in the vagina and 5% if placed into the cervix.

MATERNAL SIDE EFFECTS

Since this medicine is absorbed into your bloodstream, you may experience diarrhoea, fever or vomiting. This risk is small and your doctor may give you medicine to control some of these side effects.

UTERINE RUPTURE

There is a minimal risk of uterine rupture in women who have had prior uterine surgery. This risk is low and is something your doctor will monitor for very closely.

CORD PROLAPSE

The risks associated with amniotomy (breaking your water) include prolapse of the umbilical cord (when the umbilical cord comes out of the cervix). This usually will lead to a caesarean delivery. Your doctor will monitor closely for these complications.

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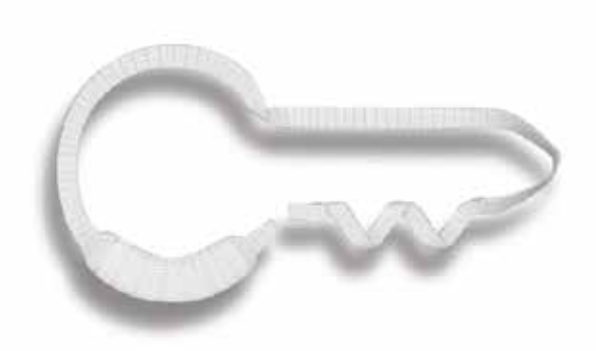
VAGINAL PESSARY



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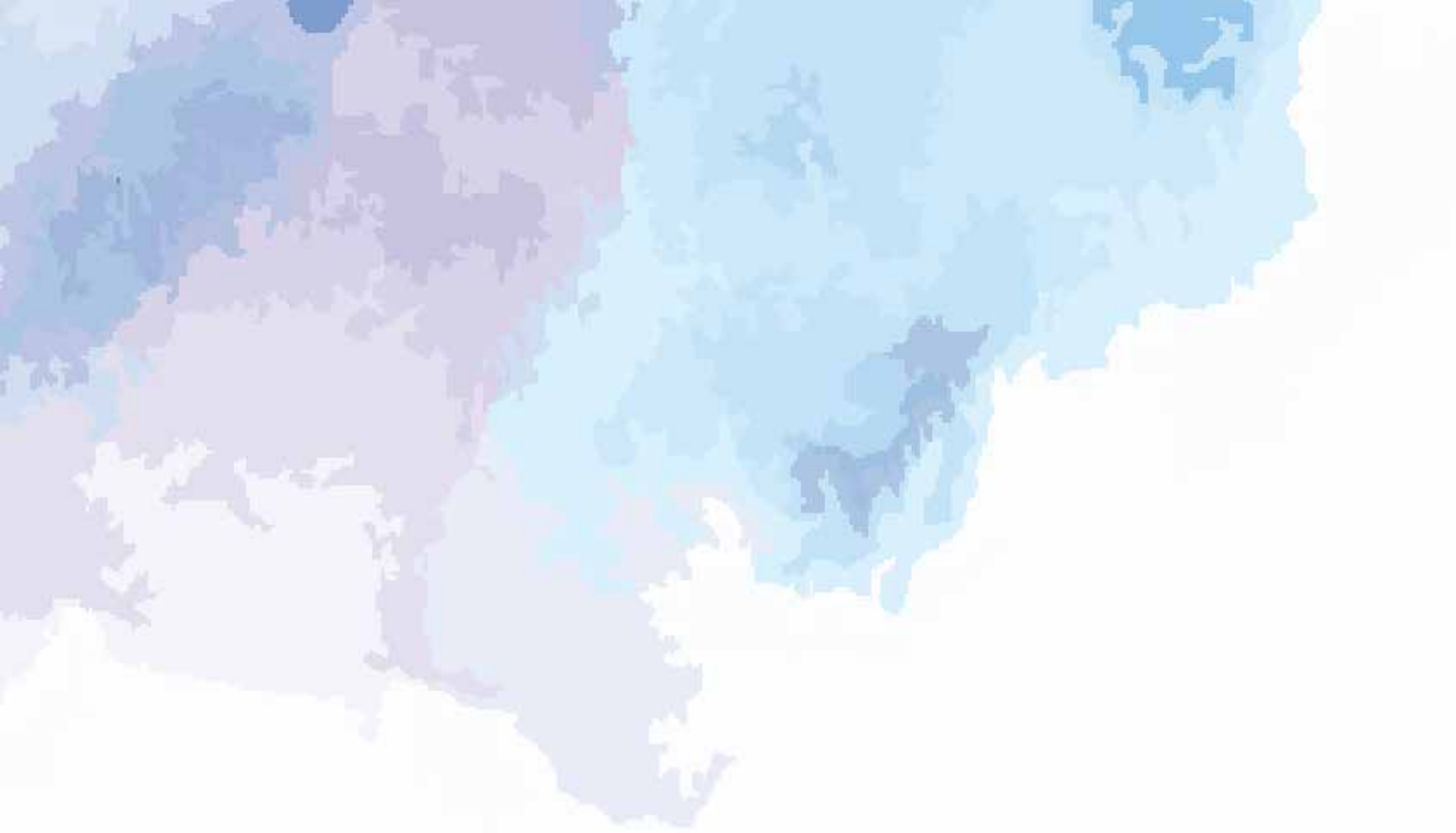

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