Lecture 15

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LABOR INDUCTION GUIDELINES
DEFINITION

Artificial stimulation of uterine contractions before spontaneous onset of labour with the purpose of accomplishing successful vaginal delivery
Structures of the cervix and Physiology of cervical ripening:

The uterine cervix has broadly two components which are:

a) cellular portion and,
b) extracellular matrix

The distal portion has greater connective tissue as compared to the part close to the myometrium which is richer in the cellular component.

The cellular component has: smooth muscle cells, fibroblasts, epithelium, and blood vessels. Cervical stromal cells produce collagenases, elastases and metalloproteinaeses which are involved in remodeling of the cervix. Fibroblasts also secrete cytokines like interleukin 1 beta and interleukin -8
Extracellular matrix is composed of:

a) **Collagen**: collagen is in two forms Type I (70%) and type II (30%) and is arranged in the form of a triple helix. In the non-pregnant cervix these are arranged in a dense and irregular fashion.

b) **Elastin**: these fibres are arranged parallel to and between the collagen fibres and play an important role in taking the pregnancy to term by keeping the os closed.

c) **Decorin**: is a glycosaminoglycan and its relative proportion to collagen is important in the remodeling of the cervix at labor.

d) **Hyaluronic acid**: is the most important proteoglycan which is responsible for the increased water content of the cervix.
Changes during pregnancy:

a) Collagen is reorganized and consolidated in early pregnancy with proliferation and hyperplasia of the cellular component
b) Near the onset of labor, an overall decrease in the concentration of collagen occurs with dispersion and remodeling into fine fibres, making the cervix softer in consistency
c) Increases in decorin levels and physiologic cell death are in part responsible for this process
d) Hyaluronic acid levels increase thereby increasing the water content of the cervix and causes a loosening and dispersal of the fibres
e) Chemotactic response at term leads to an influx of neutrophils and an increased levels of cyokines (interleukin 1 beta and interleukin –8 ) which in turn release collagenases and elastases to allow effacement
f) Mechanical forces of uterine contractions extend the elastin and allow dilatation
Indications and Contraindications

- Abruptio placentae
- Chorioamnionitis
- Fetal Demise
- Gestational Hypertension
- Preeclampsia, eclampsia
- PROM
- Postterm Pregnancy
- Maternal medical conditions
- Fetal compromise eg IUGR
- Logistics

- Vasa previa
- Complete placenta previa
- Umbilical cord prolapse
- Previous classical C/S
- Active genital herpes
- Previous myomectomy entering endo. cavity
What criteria should be met before the cervix is ripened or labor is induced?
Criteria

- Assessment of gestational age, how?
- Consideration of potential risks to mother or fetus
- Appropriate counseling including C/S risk
- Assess cervix, pelvis, fetal size and presentation
- Monitor FHR and uterine contractions
- Have physician capable of C/S readily available
PRE INDUCTION CERVICAL ASSESSMENT: It is known that success of labor induction is closely related to ripeness of the cervix. Various scores have been proposed to evaluate the cervical status.

a) **Bishop’s Score**: This was proposed by Bishop in 1964 (3) and is the most widely used score. It was originally proposed to determine the suitability of a patient for IOL in patients who were parous, at term, had an uncomplicated pregnancy and the fetus was in cephalic presentation.
Bishops scoring system

<table>
<thead>
<tr>
<th>Parameter/Score</th>
<th>0</th>
<th>1</th>
<th>2</th>
<th>3</th>
</tr>
</thead>
<tbody>
<tr>
<td>Position</td>
<td>Posterior</td>
<td>Intermediate</td>
<td>Anterior</td>
<td>-</td>
</tr>
<tr>
<td>Consistency</td>
<td>Firm</td>
<td>Intermediate</td>
<td>Soft</td>
<td>-</td>
</tr>
<tr>
<td>Effacement</td>
<td>0-30%</td>
<td>31-50%</td>
<td>51-80%</td>
<td>&gt;80%</td>
</tr>
<tr>
<td>Dilation</td>
<td>0 cm</td>
<td>1-2 cm</td>
<td>3-4 cm</td>
<td>&gt;5 cm</td>
</tr>
<tr>
<td>Fetal Station</td>
<td>-3</td>
<td>-2</td>
<td>-1, 0</td>
<td>+1, +2</td>
</tr>
</tbody>
</table>
Burnett (5) later on modified the original Bishop’s score giving a maximum score of 2 to each of Bishop's five categories, giving a total maximum score of 10.

He considered effacement in terms of length and not percentage and considered previous term birth and cephalic presentation to be pre-requisites for induction.
* Outcome of patients with a score of less than 6 was unfavorable, with a score of 9-10 all patients could be delivered within 4 hours and most within 24 hours.

Evaluating the performance of Bishop's score, Lange et al (6) observed that cervical dilatation was twice as important as the other factors and proposed a modification of the original score which predicted successful induction equally well.
Methods for cervical ripening and IOL?
METHODS OF CERVICAL RIPENING AND LABOR INDUCTION: Cervical priming before labor induction in an unfavorable cervix increases the success rates and shortens the induction to delivery interval. Methods for cervical ripening and labor induction can be broadly classified as:

- Pharmacological methods (Prostaglandins, Oxytocin & others)
- Non pharmacological methods (Natural, Surgical, Mechanical and others)
PHARMACOLOGICAL METHODS

PROSTAGLANDINS:

PG E2 gel has been widely used for pre-induction cervical ripening. Local applications of PGE2 causes cervical ripening by three mechanisms:

• Alteration of extracellular grounds substance of cervix by increasing collagenase, elastase, glycosaminoglycans, dermatan sulfate, and hyaluronic acid levels
• Relaxation of smooth muscle of cervix
• Gap junction formation leading to initiation of uterine contractions
Preparations available, Dosage and Usage Guidelines:

**Intracervical PGE2 gel:** (Cervigel, Dinoripe, Prepidil)

- Contains 0.5 mg of PGE2
- Bring the gel to room temperature before use and instill in the cervical canal below the internal os
- The patient lies supine for 15-30 minutes after the insertion.
- If no response occurs in one use a repeat insertion may be required after 6 hours.
- Maximum of 1.5 mg or three insertions are allowed over a period of 24 hours.
- If required oxytocin is to used only after 6-12 hours of the last insertion.
Intravaginal PGE2 gel:
• Vaginal PG E2 gel: contains 2.5 mg PGE2
  - 2 doses 6 hours apart are used
• Vaginal controlled release insert: (Cervidil)
  - 10 mg insert which releases 0.3 mg/hr of the prostaglandin
  - No need to pre warm the insert.
  - The patient should lie supine for 2 hours following the insertion.
  - The insert is to be removed after 12 hours or when active labor begins or in case of hyperstimulation.
Anterior Cross-Section View

- Posterior fornix
- Cervidil pessary (vaginal insert)
- Cervix
- Withdrawal tape
Contraindications:

Established uterine activity, glaucoma, asthma, severe hepatic or renal impairment, known hypersensitivity to prostaglandins, active vaginal bleeding
Side Effects

Uterine tachysystole has been reported to follow vaginally administered prostaglandin E2 in 1 to 5 percent of women. Although definitions may vary among studies, most use the terms defined by the American College of Obstetricians and Gynecologists (1999a) to describe increased uterine activity as follows:

1. **Uterine tachysystole** is defined as 6 contractions in a 10-minute period.
2. **Uterine hypertonus** is described as a single contraction lasting longer than 2 minutes.
3. **Uterine hyperstimulation** is when either condition leads to a nonreassuring fetal heart rate pattern.

Because hyperstimulation that can cause fetal compromise may develop when prostaglandins are used with preexisting spontaneous labor, such use is not recommended. If hyperstimulation occurs with the 10-mg insert, its removal by pulling on the tail of the surrounding net sac will usually reverse this effect. Irrigation to remove the gel preparation has not been helpful.
Bishop’s score should be less than 4. Drug should be administered near the delivery suite. Patient should lie recumbent for 30 minutes after the instillation. FHR and uterine activity should be monitored for 30 minutes to 2 hours after the instillation. After this, patient may be transferred elsewhere, if there is no increase in uterine activity and FHR is normal. The controlled release insert should be removed at the onset of labor. Oxytocin should be avoided for initial 6-12 hours.
Intravaginal PGE2 should be used in preference to intracervical preparations as they are equally effective and administration of intravaginal PGE 2 is less invasive of the vaginal preparations. Tablets should be preferred over the gel as they are more cheap and equally effective.
Mioprostol is a synthetic PG E1 analogue which has been used as a gastric cytoprotective agent since 1988 for patients of peptic ulcer.

Studies in late 1980’s and early 1990’s noted that oral administration of this drug causes uterine contractions in early pregnancy. Subsequent studies showed that intravaginal misoprostol causes first and second trimester abortion and there has been recent evidence of its use for cervical ripening and labor induction.
Dosage schedules and usage guidelines:

• Cheap drug
• Does not require storage conditions
• Can be given by oral, buccal or vaginal routes although vaginal route is the most extensively used
• Tablets are available as either 100 mcg or 200 mcg
• Dosage: 25 – 50 mcg is administered 4-6 hourly
• The tablet is inserted into the posterior vaginal fornix, one may or may not wet the tablet with saline prior to insertion
Misoprostol: Controlled trials: some observations: (18)

• Oral route is not recommended at this point of time
• Misoprostol shortens the Induction delivery interval as compared to PG E2 and oxytocin
• It effectively lowers the cesarean rates
• However it is not recommended as an outpatient setting or with previous C. S.
• An increase in the incidence of meconium staining of amiotic fluid and tachysystole is noted
• Overall the use of misoprostol is not associated with an increased rate of operative intervention for fetal distress and NICU admission.
ACOG guidelines

25mcg should be the initial dose for labor induction at term, should not be administered more frequent than 3-6 hours, oxytocin should not be administered < 4 hours after the last misoprostol use and the drug should be avoided in patients with previous cesarean delivery or major uterine surgery.

Use of higher dosage 50 mcg may be appropriate in some situations and have a greater likelihood of vaginal delivery within 12 hours, such doses increase the risk of hyperstimulation and rupture.

There is at present insufficient clinical evidence to address the safety of misoprostol in patients with multiple gestations and suspected fetal macrosomia.
Misoprostol appears to be more effective than oxytocin or vaginal PG E2 in presence of ruptured membranes for induction of labor.

Use of misoprostol in obstetrics must be restricted to RCTs.

Oral misoprostol appears to be less effective than vaginal misoprostol, however, oral route is associated with less incidence of uterine hypercontractility but a higher incidence of meconium stained liquor.

Its use is associated with increased uterine hypercontractility but this is not translated in increased operative delivery rates. The safety issues surrounding the use of misoprostol have not been clearly evaluated.

* Despite a lot of clinical use, misoprostol is still not approved by the Drug Controller of India for use in induction of labor.
OXYTOCIN:

Oxytocin is a polypeptide hormone secreted from the posterior pituitary gland which acts as a potent uterotonic agent. The drug was used intravenously in 1948 by Theobald et al (21) to induce labor. Later in 1958 Du Vigneaud et al (22) synthesized the drug. Since then it has been the most commonly used drug for induction and augmentation of labor.

Routes of administration:

Oxytocin can be administered by any parenteral route, intravenous route being the most widely used. It can be absorbed from the nasal or buccal mucosa, however when given orally it is rapidly inactivated by trypsin.
Dosing and Usage Guidelines:

10 –20 units are dissolved in 1000 ml of balanced salt solution ( Ringer Lactate solution or Normal saline ) making it as 10-20 mu/ml and it is preferable to give it through an infusion pump. Further increments are made according to the low dose or high dose protocol given below (15 ) :

<table>
<thead>
<tr>
<th>Regimen</th>
<th>Starting dose (mU/ min)</th>
<th>Incremental dose (mU/ min)</th>
<th>Dosage interval (min)</th>
</tr>
</thead>
<tbody>
<tr>
<td>Low Dose</td>
<td>0.5 – 1</td>
<td>1</td>
<td>30-40</td>
</tr>
<tr>
<td></td>
<td>1 – 2</td>
<td>2</td>
<td>15</td>
</tr>
<tr>
<td>High dose</td>
<td>6</td>
<td>6</td>
<td>15</td>
</tr>
<tr>
<td></td>
<td>6</td>
<td>6, 3*, 1*</td>
<td>20-40</td>
</tr>
</tbody>
</table>

* The incremental increase is reduced to 3 mU/min in presence of hyperstimulation and reduced to 1mU/min with recurrent hyperstimulation.
After intravenous infusion, uterine response occurs within 3-5 minutes and a steady state plasma concentration is reached in about 40 minutes.

The end point to be achieved is uterine contractions every 2-3 minutes lasting for 40-45 seconds and a uterine pressure of 50-60 mm Hg or 150 Montevideo units.
Risks of Oxytocin:

- Hyperstimulation, with or without fetal heart rate changes
- Failed induction with need for repeat induction or possibly cesarean
- Increased risk for uterine rupture in some studies
- Hypotension if administered by IV bolus
- Hyponatremia if administered with large amounts of sodium poor fluids
- Antidiuretic hormone like effect if administered at high doses
- Increased risk for neonatal hyperbilirubinemia
CONTRA-INDICATIONS:

Contraindications include but are not restricted to:

1. Unfavorable fetal positions

2. Uterine tachysystole

3. Hypersensitivity to the drug

4. Cases where vaginal delivery is contraindicated, such as complete placenta previa, vasa previa, and cord prolapse
Other Pharmacological methods:

a) **Mifepristone**: 200 mg misoprostone for 2 days has been recently used for cervical priming (23). However this method is not cost effective and needs further trials.

b) **Relaxin**: Relaxin has been demonstrated to causes changes in the collagen resulting in cervical softening. Both purified porcine and DNA produced human relaxin have been tried with success in promoting cervical ripening with no adverse maternal and fetal outcomes (24,25). It is not yet commercially available.

c) **Nitric Oxide**: Animal studies have shown it to be a cervical ripening agent but it is unlikely to be used for human use unless safety of NO in late pregnancy is established.

d) **Cytokines**: Theses are chemotactic agents which also can promote cervical ripening by causing changes in the extracellular matrix.
AMNIOTOMY: Ideally amniotomy or ARM is performed when the cervix is effaced and 2 cm dilated but it can be performed with minimal cervical dilatation.

Methodology of ARM:

- Auscultate the FHR
- Evaluate the cervix and station of head. The cervix should be well applied to the head
- Introduce two fingers into the cervix, sweep away the membranes from the cervix
- Pass an Allis or Kocher’s forceps in between the groove of your two fingers, hook the membranes and rupture them; look for the clarity of liquor
- Risks: Cord prolapse
  - FHR deceleration
  - Bleeding through vasa praevia
  - Fetal injury
    - Maternal and fetal infection
- Advantages:
  - It shortens duration of labor
  - Allows for early diagnosis of meconium staining of amniotic fluid, specially in high risk pregnancy
  - Facilitates invasive fetal monitoring
**MECHANICAL MODALITIES:**

_a) Hygroscopic dilators:_ These are natural or synthetic rods inserted through the cervical os and left in situ for a particular time wherein because of their osmotic properties they absorb endocervical and local tissue fluids. This swelling causes a controlled dilatation of the cervix along with releasing prostaglandins. Natural dilators are obtained from the seaweed *Laminaria japonicum._

_b) Balloon devices:_ Foley’s catheter or designer balloon devices when inserted intracervically can facilitate cervical ripening. Once properly placed (beyond the internal os) balloon or the catheter is inflated with 30-50 ml saline. It is recommended to either attach a defined weight to the catheter end (1litre of i.v. fluid) or to use “gentle tugs” – 2 to 4 each hour until the catheter or the balloon passes out (26,27). Some recommend infusion of extra-amniotic saline at the rate of 1 cc/minute. There is no infection associated with balloon devices.
Mechanical – Double balloon
MISCELLANEOUS:

a) Castor Oil (28) : It is an extract from “Ricinus communis” and is mainly crude ricinoleic acid. It is known to stimulate gut peristalsis and labor most likely is stimulated due to release of prostaglandins. The method is no longer used now. One study has reported an increased incidence of meconium staining of amniotic fluid.

b) Accupuncture and TENS( Transcutaneous electric nerve stimulation) : Few studies (29-31) have reported successful induction of labor with these methods but further trials are needed before planning a large scale use.
CERVICAL RIPENING AND IOL IN SPECIAL CIRCUMSTANCES:

a) Previous C. S.:

- One or more previous C. S. are not a contraindication to the induction of labor.
- Cervical ripening can be done in these situations with PGE2 gel – either intravaginal or intracervical.
- Misoprostol is an absolute contraindication.
- Oxytocin can be safely used in low doses with close monitoring of uterine contractions and FHR.
- It is preferable to have continuous electronic fetal monitoring.
b) Twin pregnancy:
- PGE 2 gel can be safely used for cervical ripening
- ARM facilitates induction
- Oxytocin in low doses can be used

c) **Premature rupture of membranes (PROM)**:
- Use of PGE2 gel—2 doses 6 hours apart is not associated with higher incidence of infection
- Misoprostol can also be used in 25 mcg dose
- Oxytocin infusion should be closely monitored
- Beware of hyperstimulation
d) **Intrauterine fetal demise (IUFD):**

- Oxytocin is effective for IOL near term with a favorable cervix.
- All prostaglandins can safely be used in recommended dosages for cervical ripening remote from term.
Failure of Induction

It is defined when Cx failed to dilate up to 3-4 cm in 24 hrs of induction.
What to do now?
- Option to wait-- if No PROM and postponement is not harmful for fetus as well as mother.
- Review the case and if there is urgency, Caesarean delivery is performed.
RISKS OF INDUCTION

- Failure leading to CS
- Uterine hyperstimulation
- Fetal distress, death
- Rupture uterus
- Intrauterine infection, sepsis
- Iatrogenic delivery of preterm infant
- Precipitate/dysfunctional labour
- Inc. risk of operative vaginal delivery
- Inc. risk of birth trauma
- Inc. risk of PPH
THANK YOU