Labour Induction Methods: An Overview

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Authors’ contributions

This work was carried out in collaboration between both authors. Both authors read and approved the final manuscript.

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ABSTRACT

Overall the rate of induced labours has increased and almost 25% of women undergo labour induction worldwide. Cervical ripening and cervical preparedness is necessary before labour can be induced. The status of the cervix is traditionally assessed with help of Bishop's score. Labour induction becomes necessary when the cervix is not favourable as noted on the cervical scoring system. Mechanical or surgical methods or a combination of both can be sued for labour induction. These include Foley's catheter induction, sweeping of membranes, amniotomy etc. Pharmacological agents like oxytocin, prostaglandins PGE1 & PGE2 and newer agents like mifepristone can be used. Mechanical methods like Foley's catheter induction are associated with lesser FHR variability and decreased rates of caesarean section as compared with oxytocin infusion or prostaglandins used locally. Oxytocin is the most widely used pharmacological method used for induction of labour. Proper titration of oxytocin can result in contractions that mimic normal labour. Oxytocin is often combined with amniotomy. Prostaglandins PGE1 & PGE2 are safe and effective options for labour induction. Prostaglandin PGE1 or misoprostol is used in the dose of 25 microgram mcg given orally or vaginally or via the sub-lingual route. Prostaglandin PGE2 or dinoprostone is used intra-cervically or vaginally in the posterior fornix. The newer drug mifepristone is being studied as cervical ripening agents because of its anti-progesterone effect.

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1. INTRODUCTION

Almost 25% of all gravid women undergo labour induction and the overall rate of induced labor has almost doubled in the last decade [1]. The purpose of induction of labour IOL is to artificially stimulate the uterus to start contractions before onset of spontaneous labor pains. Labor induction should be undertaken when it is clear that delivery will be beneficial for the mother and baby as compared to continuation of pregnancy [2]. It should be used with caution in cases of previous caesarean section and multigravida.

Cervical ripening or preparedness for induction is necessary for successful vaginal birth. Cervical ripening is the process where the cervical softens, thins out and dilates, and this helps reduce induction to delivery interval. Cervical remodelling is essential process for beginning of normal labour. The changes include breakdown of collagen and changes in the glycosaminoglycans while also increasing the production of cytokines [3]. The condition of cervix is assessed with the help of a pelvic scoring system called Bishop’s score (Table 1) [4]. The cervix is considered to be unfavourable when the Bishop score is less than 6. A score is more than 8 is said to be favourable and the chances of vaginal delivery are high after labor induction [5] (Table 1).

IOL becomes necessary when the cervix is not favourable, and for this various cervical ripening agents can be used. Non-pharmacologic agents for achieving cervical priming and IOL have been popular since ancient times. They include herbs and herbal remedies, hot baths, enema, use of castor oil and such measures like sexual intercourse & nipple or breast stimulation. Procedures like acupressure, acupuncture & transcutaneous nerve stimulation TENS may also be helpful. Thereafter came the mechanical and surgical methods of labour induction [6,4,7-9]. From amongst the non-pharmacologic methods, mechanical and surgical methods are currently being used widely and have proven to be helpful ripening of the cervix. Currently the medications used for ripening of the cervix are oxytocin, prostaglandins PGE1 & PGE2, and newer agents like mifepristone. The most popular pharmacologic method used for IOL is oxytocin. The use of the posterior pituitary extract for labour induction was first described by Theobald [10]. Exactly five years later, oxytocin was discovered by Vigneaud et al. [11].

2. NON-PHARMACOLOGIC METHODS

Non-pharmacologic methods of induction of labour

2.1 Mechanical Methods

Mechanical methods are being used since long time and are useful for priming of the cervix. They include -1) Hygroscopic materials like Laminaria tents - These are not used nowadays as there is not much evidence regarding the use of osmotic dilators for pre-induction cervical ripening.

2) Foley’s catheter is the frequently used as mechanical method for induction. Foley’s catheter with bulb inflation of 30–80 mL give best results. Foley’s catheter induction is popular because of comparatively low cost and decreased incidence of hyper stimulation. Foley’s catheter acts by mechanical stretching of the cervix caused by catheter balloon. Placement of catheter causes release of prostaglandins and causes cervical ripening. Thus Foley’s catheter leads to changes in biochemical mediators resulting in cervical ripening [12]. The intra-cervical catheter will fall out spontaneously within 24 hours. Foley catheter can be followed up with oxytocin infusion if required for induction of labor. It is contraindicated in cases of placenta praevia and in women with ruptured membranes.

| Cervix          | 0     | 1     | 2     | 3     |
|-----------------|-------|-------|-------|-------|
| Position        | Posterior | Mid-position | Anterior | -     |
| Consistency     | Firm  | Medium| Soft  | -     |
| Effacement      | 0-30% | 40-50%| 60-70%| >80%  |
| Dilation        | Closed| 1-2 cm| 3-4 cm| >5 cm |
| Baby’s station  | -3    | -2    | -1    | +1, +2|
Mechanical methods are associated with a lesser fetal heart variability & decreased caesarean section rates as compared to oxytocin infusion or prostaglandins [13,14,15]. Balloon catheters are less likely to cause hyper stimulation of the uterus and hence IOL with catheter placement is preferred for women with scarred uterus/previous CS. Systematic reviews have compared mechanical methods like Foley's catheter with local prostaglandins like misoprostol and cervical dinoprostone. They found that mechanical methods had longer ripening to delivery interval as compared to cervical and vaginal prostaglandins. However rates of uterine hyper stimulation were more with prostaglandins than with mechanical methods [16, 17].

3) Double balloon devices (Atad Ripener Device) – In 2005 US FDA approved the ‘Atad Ripener Device’. This catheter has double balloons with capacity of 80 ml each. The double balloon devices seem to be better than Foley’s catheter, as the forces act on both sides of the cervical os. [18]. Studies have not shown much variation in caesarean section rates between women having induction with mechanical methods and those women who received placebo/no treatment. Women subjected to mechanical methods required oxytocin augmentation more commonly.

3. MEMBRANE SWEEPING OR STRIPPING

Sweeping of membranes or stripping is mostly the first step of labor induction. This causes release of prostaglandins from the membranes and decidua and leads to increase in phospholipase A2 activity and levels of prostaglandin PGF2α [19]. It may also lead to release of oxytocin from the post pituitary by Ferguson’s reflex. Stripping of membranes by itself increased the chances of spontaneous labor pains and other methods of induction were not frequently needed [20]. No difference was found in rates of caesarean sections, perinatal deaths or serious neonatal infections associated with stripping of membranes. Sweeping lessens the risk of pregnancies going post-dated [21].

Stripping of the membranes is not useful for urgent indications of induction as the interval between sweeping of membranes and beginning of labor pains can be longer as compared to other methods of cervical ripening. However it can be used as an adjunct to pharmacological methods like oxytocin [22]. Drawback of stripping the amniotic membranes is that it can cause bleeding from an undiagnosed placenta prævia and amniotic membranes can be ruptured accidently.

4. AMNIOTOMY

Amniotomy is the procedure where membranes are ruptured artificially for achieving induction of labour. Amniotomy is useful for inducing labor when the status of the cervix is favourable. Also amniotomy by itself, is not recommended for labour induction, as this can be associated with long induction to delivery intervals [23]. Studies have compared amniotomy alone or combined with oxytocin, with placebo or with prostaglandins. Amniotomy when combined with oxytocin, resulted in decreased cases of meconium staining of liquor and also shortened induction-to-delivery intervals leading to more women delivering within 24 hours [24, 25]. It is specially indicated in conditions like abruptio placentae, hypertensive disorders and post-maturity. The complications that can be caused by amniotomy are cord prolapse, infection, injury, amniotic fluid embolism and iatrogenic prematurity. Contraindications are immunodeficiency and genital herpes infection.

5. PHARMACOLOGICAL METHODS

Pharmacological methods of induction of labour

1) Oxytocin Oxytocin is the most popular and time tested drug for inducing labours worldwide. Oxytocin is a naturally occurring nonapeptide which arises from the hypothalamus and is let down from the posterior pituitary gland. Its acts on oxytocin receptors of the uterus and thereby induces uterine contractions but does not have much effects on the cervix [26]. Sensitivity to oxytocin is increased in the third trimester and is maximum at term. The response of the uterus to oxytocin depends on various factors like, gestational age, maternal age and parity, BMI and degree of cervical dilatation. Response of uterus to oxytocin begins within few minutes of starting infusion, and constant levels of oxytocin are reached within 30-40 minutes.

Different strengths of oxytocin can be used for oxytocin intravenous infusion like 2 IU, 5 IU or 10 IU of oxytocin added to 500 ml of normal saline solution. It can be started at the rate of 1–2 milliunits/minute mU of oxytocin per minute, and
then increased every 20 – 30 minutes. It may be gradually increased at rate of 1 to 4 milliunits/minute approximately till uterine contractions mimicking normal labour are established. The maximum licensed dose is 20 mU per minute, although many units use up to 32 mU per minute [27]. It is necessary that oxytocin is used judiciously, because of risk of hyperstimulation and FHR changes [28]. Immediately after starting intravenous oxytocin drip, the oxytocin infusion rate should be monitored closely. Maternal condition is monitored particularly pulse and blood pressure. Monitoring of FHR and uterine response to oxytocin is done. Partogram should be used for monitoring the progress of labour. Specific guidelines for oxytocin use in labour induction is described in WHO manual [29].

Cochrane review was done to study oxytocin alone for induction of labour [30]. Comparison was done between oxytocin used alone and placebo/expectant management. Oxytocin alone was associated with decreased rate of caesarean section and fewer admissions to NICU. Various studies showed that oxytocin was more effective as compared to placebo, but was less effective when compares with prostaglandins for achieving vaginal delivery. The incidence of caesarean sections was more with oxytocin than with prostaglandins. Successful vaginal delivery was achieved within 24 hours when intravenous oxytocin was combined with amniotomy. Caution is advised when using oxytocin in women with prior caesarean delivery and multiparous women because of risk of uterine rupture.

2) Prostaglandins-They cause changes that promote ripening of the cervix and lead to increased uterine contractility. Prostaglandins are contraindicated for IOL in women with prior caesarean births. Prostaglandins can be associated with side effects like fever with chills, diarrhoea & vomiting and can cause hyperstimulation of uterus. The route of administration, frequency and dosage and the type of prostaglandins used for cervical ripening can vary at different centres.

**Prostaglandin pge1 –misoprostol oral prostaglandins:** Misoprostol is a synthetic PGE1 analogue which is safe and effective for ripening of cervix and labour induction. Misoprostol is presently available in the form of 100 microgram mcg and 200 mcg tablet, which can be cut to pieces for providing smaller doses of 25 or 50 mcg doses. It can be given orally, vaginally, or via the sublingual/buccal route and is used both for ripening of cervix and IOL [31,32]. Misoprostol has been approved for use in gastric ulcer disease resulting from use of NSAID’s. Use of the drug for ripening of cervix is considered as off-label use. Misoprostol is used in dose of 25 mcg initially, and then at intervals of two to six hours. Oxytocin may be started four hours after the final dose of misoprostol. The dosage and frequency of intra-vaginally used misoprostol can be variable [33, 34].

The WHO World Health Organization has recommended dose of 25 mcg every two hours [35, 36]. Cochrane reviews have supported using oral misoprostol rather than vaginal misoprostol for ripening of unfavourable cervix. Misoprostol administered orally was found to be more effective than placebo, and resulted in decreased rate of caesarean sections when compared with vaginal misoprostol/dinoprostone gel. Studies recommend the use of 25 microgram of misoprostol as oral solution [30].

Oral misoprostol was found to be effective as a labour inducing agent for achieving vaginal birth. Comparison between placebo/expectant management and oral misoprostol, found oral

**Table 2. Oxytocin titration table**

| Units of oxytocin mixed in 500 ml ringer solution | Drops per minute (15 drops = 1ml) |  |  |
|--------------------------------------------------|----------------------------------|---|---|
| 1 unit = 1000 milliunits (mU)                    | 15                               | 30 | 60 |
| In terms of mU /min                              |                                  |    |    |
| 1                                                | 2                                | 4  | 8  |
| 2                                                | 4                                | 8  | 16 |
| 8                                                | 16                               | 32 | 64 |

*Note: In majority of cases, max, response is seen with 16 mU /min i.e. 2 U in 500ml RI at 60 drops per min.*
misoprostol to be more useful for achieving successful vaginal delivery within 24 hours. When oral versus vaginal misoprostol were compared, oral misoprostol was found to be more useful. (Thomas et al., 2014) (French, 2001) (Boulvain et al., 2008). There were fewer caesarean sections and better maternal and perinatal outcomes with oral misoprostol as compared to dinoprostone gel or oxytocin. FHR abnormalities and uterine hyper stimulation were lesser with misoprostol given orally as compared to vaginal route [37].

Oral misoprostol is especially useful when there is risk of ascending infection as in PROM, and also when there is shortage of hospital staff because supervised self-administration can be done by the patient (Alfirevic et al., 2014). Most of the adverse maternal and fetal outcomes were found when misoprostol was used of doses greater than 25 mcg. Misoprostol in higher doses of 50 mcg every 6 hours, may be required in some situations. However higher doses can be associated with an increased risk of complications, including uterine hyper stimulation and FHR abnormalities.

Prostaglandin Pge1 - Vaginal Prostaglandins: It was recommended that prostaglandin PGE1 be used as 25 mcg tablet intra-vaginally at interval of 3-6 hours [38]. Higher doses may be associated with a risk of side effects mainly the risk of hyper-stimulation. Hyper stimulation is defined as contractions that are greater in duration and intensity, lasting for more than 60 seconds and frequency of more than 5 in 10 minutes. Goldberg defined tachysystole as contractions lasting more than 6 in 10 minutes, observed during two consecutive periods of 10 minutes. Hyper-systole was diagnosed when a single contraction lasted for 2 minutes [38]. Several RCT’s have shown that misoprostol (PGE1) is an effective method for ripening of cervix. Intra vaginal misoprostol was found to be equally effective as dinoprostone gel [39].

Prostaglandin PGE2 - Cervical Prostaglandins: Prostaglandin PGE2 used locally probably increases the chances of cervical dilatation and vaginal delivery. Prostaglandin PGE2 can be used in tablet form or as gels and pessaries as all formulations seem to be equally effective. PGE2 is available as 0.5 mg of dinoprostone gel as prefilled syringe with inserter. It is intracervically or vaginally in the posterior fornix. Dinoprostone tablets 500 mcg can be given vaginally. Vaginal inserts are available in some countries and contain a controlled-release, retrievable polymer chip which gradually releases 200 mcg over 24 hours. PGE2 may be associated with increased chances of hyper stimulation of the uterus and FHR abnormalities, however there is not much effect on caesarean section rates [40]. Use of intra-cervical or intra-vaginal PGE2 (dinoprostone), was found to be superior to placebo/no therapy for inducing ripening of cervix [41,42].

Various studies compared vaginal misoprostol with sublingual/buccal misoprostol. The studies showed that use of vaginal and sublingual/buccal misoprostol both had similar outcomes. (Kelly et al., 2009) (French, 2001) (Boulvain et al., 2008) [43].

Other studies compared Foley’s catheter induction with various pharmacological methods like oxytocin, vaginal and cervical prostaglandins. PROBAAT trial (Prostaglandin or Balloon Catheter for Induction of Labour) compared prostaglandin PGE2 gel with Foley’s catheter for IOL. According to this study Foley’s catheter induction did not lower caesarean section rates. Also there was not much difference in rates of hyper-stimulation or postpartum haemorrhage. The study found that there Foley’s catheter induction did not have much advantage over prostaglandins [44].

In the PROBAAT-II trial comparison was made between oral misoprostol and Foley’s catheter for the purpose of labour induction. Vaginal delivery occurred more commonly within 24 hours when labour was induced with oral misoprostol than with Foley’s catheter. Caesarean section rates between misoprostol and Foley’s catheter group were comparable. There was not much difference in rates of hyper stimulation or FHR changes. The study concluded that effectiveness and safety of oral misoprostol was similar to that of Foley’s catheter for labour induction [45].

The PROBAAT-P trial tried to compare use of prostaglandin E2 10 mg as vaginal inserts with Foley’s catheter for labour induction. Meta-analysis showed that Foley’s catheter had lesser chances of hyper stimulation. The incidence of caesarean sections was comparable in the two groups. Also admissions to the NICU and perinatal outcomes were similar in both groups. Thus both groups demonstrated comparable results [46].
Comparison between Foley’s catheter and PGE2 gel found no differences in the duration of induction to delivery interval. However PGE2 was associated with a higher risk of hyper stimulation and FHR abnormalities as compared to the Foley’s catheter [15].

3) Mifepristone Mifepristone can be used for ripening of cervix because of its anti-progesterone effect. Progesterone is known to inhibit the contraction of the uterus, while mifepristone induces contraction of the uterus. Currently there are studies being conducted to study the use of mifepristone for cervical ripening. The recommended dose of 400 mg mifepristone is sufficient for causing the necessary cervical changes needed for labor induction [47].

Systematic review studied mifepristone for IOL. It included 10 trials which studied 1108 women. [48]. The study concluded that mifepristone was better than placebo for achieving cervical ripening and starting of labour pains. Compared to placebo, mifepristone decreased the chances of caesarean section, but there was increased risk of instrumental deliveries. However neonatal outcomes were not adversely affected. Not much information is available regarding the maternal and fetal outcomes and safety of mifepristone. Hence routine and active use of mifepristone is not recommended for cervical ripening [49].

4) Relaxin: It is thought that the hormone relaxin promotes ripening of the cervix. However there is lot of debate regarding the use of relaxin as agent for cervical ripening. It possibly has an inhibitory effect on the myometrium. Comparison between relaxin and placebo/no treatment, revealed that relaxin was better for ripening of the cervix. However some women receiving relaxin, needed augmentation with oxytocin or prostaglandins. The study found that there were no differences in caesarean section rates in women who received relaxin as compared to women who received placebo. Chances of hyper stimulation and FHR changes were less as compared with other agents. However there is insufficient data available, regarding perinatal outcomes [50].

Other Cervical Ripening Agents: Other cervical ripening agents like nitric oxide donors [51], hyaluronidase [52], corticosteroids [53] have been studied. However because of availability of limited data regarding safety and efficacy these methods cannot be recommended for routine use [54-57].

6. CONCLUSION

Almost 25 % women have their labours induced worldwide. Oxytocin is the most popular and time tested medication for induction of labour. Prostaglandins are effective for causing cervical ripening and also for inducing labor. Vaginal misoprostol is a very effective method of IOL even when Bishop Score is unfavourable. An initial dose of 25 mcg of misoprostol approximately should be used for priming of cervix and IOL. 25 mcg of misoprostol can be repeated every 2–6 hours. Misoprostol should be used with caution in women with prior caesarean deliveries and in women with history of major uterine surgery. There is associated risk of increased chances of uterine rupture. The Foley’s catheter induction can be reliable and safe alternative for cervical ripening and IOL. Newer agents like mifepristone are being studied for use as cervical ripening agents.

CONSENT

It is not applicable.

ETHICAL APPROVAL

It is not applicable.

COMPETING INTERESTS

Authors have declared that no competing interests exist.

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