

Induction of Labor and its Effect on Primary Cesarean Delivery: A Review

Madhu Shakya¹, Tao Duan^{1,2*}¹Department of Obstetrics and Gynaecology, Shanghai First Maternity and Infant Hospital, Tongji University School of Medicine, Changle Road 536, Shanghai 200040, China²Shanghai Woman's Healthcare Institute, Shanghai, China

Abstract

Labor induction nowadays is commonly used all over the world and it has been increasing. Researches are being done for newer and effective methods of labor induction and cervical ripening. The goal of labor induction is to achieve vaginal delivery by stimulating uterine contractions before the onset of spontaneous labor. Induction of labor is said to be successful if the cervix is ripen because it reduces the induction to delivery time and rate of failed induction. Cesarean section was thought to be increased by the use of labor induction methods but recent studies showed that neither cesarean delivery nor perinatal morbidity or mortality was increased by induction of labor. This article summarizes currently available labor induction methods and their effectiveness and safety on primary cesarean section, operative vaginal delivery, neonatal outcomes and other available evidences based on well conducted clinical trials.

Keywords: Cesarean section, double balloon catheter, foley catheter, induction of labor, misoprostol, prostaglandins.

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***Correspondence:** Tao Duan [Email tduan@yahoo.com](mailto:tduan@yahoo.com)

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Introduction

Child birth by its varying nature carries potential risks for the woman and her baby, regardless of the route of delivery [1]. Induction of labor is a method of prematurely or artificially stimulating the onset of labor prior to the onset of spontaneous labor. The labor induction rate has increased steadily, with rates more than doubling from 9.5% in 1990 [2] to 23.3% of pregnancies in 2012 [3] and this trend will continue to rise in future. WHO had published the most recent worldwide data of labor induction in 2011 showing that Niger has the lowest rate (1.4%) and Sri Lanka had the highest rate (35.5%) [4]. Labor is induced in one of five births [5,6] for maternal reasons (e.g. preeclampsia, cardiac or renal disease), fetal reasons (e.g. intrauterine growth restriction) and a combination (e.g. poorly controlled diabetes, preterm rupture of membrane, or post term pregnancy) [7].

Earlier, cesarean section (CS) was thought to be increased by the use of labor induction methods but recent studies showed that neither CS nor perinatal morbidity or mortality was increased by induction of labor [8,9,10,11]. This review encompasses 2 mechanical methods (double balloon catheter, Foleys catheter) and 2 pharmacological methods i.e. prostaglandins (PGs) including prostaglandin E1 (PGE1) and prostaglandin E2 (PGE2) for labor induction.

Cervical Ripening

Cervical ripening is the main key factor for successful labor induction. It is the process resulting in softening, effacement and dilatation of the cervix [12]. In 1964, Bishop developed a scoring system to evaluate multiparous women for elective induction at term [13]. But it has also been widely used to evaluate nulliparous women for labor induction [14]. To make it more simpler and easy to use, Bishop's scoring system has been modified and cervical effacement has been replaced by cervical length [15,16]. Higher the bishop score, more favorable is the cervix and vice versa. In a patient with unfavorable cervix (Bishop score ≤ 6), cervical ripening can help reduce induction to delivery time and the rate of failed induction [5] which in turn reduces CS. Cervical ripening can be obtained by using mechanical and pharmacological methods.

Mechanical Methods

Mechanism and its effects

Mechanical methods are one of the oldest methods used for cervical ripening. Older mechanical methods like osmotic and hygroscopic dilators, laminaria tents were associated with an increased risk of peripartum infection and are not commonly used for labor induction [17,18,19]. Nowadays, most commonly used mechanical methods are double balloon catheter and Foley catheter. These mechanical methods have

cervicovaginal balloon allowing compression at the cervical os. Due to compression at cervical os, it releases endogenous prostaglandins from the fetal membranes by stimulating uterine contractility resulting to cervical ripening [20]. They are cost effective, easy to store, have less hyper-stimulation effect and fewer side effect to mother and baby [21]. The side effects are infection, discomfort due to manipulation of cervix while inserting mechanical devices, require trained and skilled personnel to insert catheter.

Comparison between two mechanical methods

Double balloon catheter is a more recent variation of Foleys catheter for induction of labor, which has two balloons used for inflation on internal as well as external os [22]. In a pilot randomized controlled trial by Wilkinson et al [23], 48 women with low risk singleton, term pregnancies with bishop score <7 were randomly allocated to either outpatient or inpatient Cook double balloon catheter for cervical ripening. Oxytocin was required either for induction or augmentation in many women. An outpatient group required 24% less oxytocin and had a lower primary CS rate although not statistically significant. Clinical and Perinatal outcome was similar between two groups. No cases of failed induction, infections, uterine hyperstimulation, maternal and neonatal mortality were recorded. The outpatient double balloon catheter ripening can be an alternative to decrease patient anxiety and somewhat decrease the use of oxytocin and the rate of primary CS but further evaluation must be done.

In another prospective quasi randomized trial performed at Israel [24], 188 low risk women with bishop ≤ 4 were randomly selected for Cook double balloon catheter and Foleys catheter with extra-amniotic saline infusion. The insertion to expulsion time of catheter and induction to delivery time was significantly shorter in Foley catheter group. Primary CS, instrumental delivery and maternal and fetal adverse outcomes did not differ significantly in both groups although with cook double balloon catheter arrest of the first stage of labor was more common while with Foley catheter arrest of second stage of labor was more common. In this study Foley catheter seems to be superior to double balloon catheter. Another prospective randomized study by Salim et al [23] enrolled 293 low risk women with bishop score ≤ 6 undergoing labor induction with either double balloon catheter or single balloon catheter. No difference was found in induction to delivery time. But the incidence of primary CS and vacuum

delivery was lower in single balloon group than in double balloon group. In this study, it showed that single balloon catheter is more effective than double balloon catheter.

Randomized trial by Delaney et al [25] showed 199 women with a term, cephalic, singleton gestation with bishop score <5 undergoing labor induction who were randomly selected to receive Foley catheter inflated with either 30 ml or 60 ml of normal saline. Oxytocin was started 30 minutes after Foley was kept. 26% women who received Foley catheter inflated with 60 ml of normal saline delivered within 12 hours compared with 14% in 30 ml group. No differences in the induction to delivery time, delivery within 24 hours, primary CS rate and maternal or neonatal morbidity were seen in two groups. According to duration of delivery, Foley catheter inflated with 60 ml would be more effective method of induction.

Comparison of double balloon catheter with pharmacological methods

Pennell et al [26] in his study showed 330 nulliparous term women with unfavorable cervix (bishop score <4) who was randomly selected for double balloon catheter, single balloon catheter and PGE2. No differences were found in CS rates and neonatal admission rates between three groups. Induction to delivery time was longer in double balloon group than two other groups. 14% of PGE2 group had uterine hyperstimulation with none in other two groups. Though there were no differences for CS with three methods, patient comfort and safety was seen with single balloon catheter in this study. A prospective study [27] of 155 women with bishop score of ≤ 6 cm requiring labor induction at term were compared using double balloon catheter and PGE2(dinoprostone vaginal insert). There were no differences in primary CS rate, vaginal delivery rate within 24 hours and neonatal outcomes in two groups. Induction with double balloon catheter resulted in lesser uterine hyperstimulation and shorter delivery time but more frequent use of oxytocin was required [27].

Two recent study involving women with a bishop score ≤ 6 showed that higher rate of vaginal delivery within 24 hours occurred in women with unfavorable cervix especially nulliparous with the use of double balloon catheter [28,29]. In contrast, one study comparing PGE2 and double balloon catheter in patient with oligohydramnios ≤ 5 and bishop score ≤ 6 were found to have a shorter induction to delivery time in PGE2 group but CS rate and neonatal outcomes had no differences in both groups [30]. In

another multicentre randomized trial by Kehl et al [31], 326 women with unfavorable cervix of bishop score ≤ 7 underwent labor induction at term using double balloon catheter and oral misoprostol combined and oral misoprostol alone. Women receiving double balloon catheter received 50 μg oral misoprostol if labor did not start within 24 hrs of induction with mechanical method. If still labor did not start after 24 hours of oral misoprostol, 100 μg was given orally three times a day. After 48 hours of start of oral misoprostol, 100 μg was vaginally inserted 4 hourly three times a day. Oral misoprostol alone had the same protocol. The induction to delivery time was significantly higher in double balloon catheter and misoprostol group but after adjusting with parity this difference was not seen. The rate of vaginal delivery within 48 hrs and neonatal outcome was similar in both groups. This study showed that induction to delivery time and the rate of delivery within 48 hours did not improve despite of combined therapy.

Comparison of Foleys catheter with pharmacological methods

Jozwiak et al [32] performed multicentre open label randomized trial of Foley catheter and PGE2 vaginal insert where total 226 women with singleton, cephalic, term gestation, intact membrane, unfavorable cervix (bishop < 6) and no previous CS were included. CS rate were comparable (20% vs 22% respectively). No differences were seen between two groups for maternal and neonatal morbidity and induction to delivery time but in a Meta-analysis (PROBAAT-P study), comparable CS rates and less hyperstimulation was seen with the use of Foley catheter than with PGE2 vaginal insert. Jozwiak et al [33] studied comparison of Foley catheter and vaginal misoprostol for its effectiveness and safety in term 120 women for induction labor. CS rates, maternal and neonatal outcomes did not differ significantly. Time for induction to delivery and CS due to failure to progress was more seen in Foley catheter group. But meta-analysis showed no difference in CS rate, less hyperstimulation and reduced vaginal instrumental deliveries with Foley catheter resulting in superiority of Foley catheter over misoprostol.

A randomized study done by Nasreen and colleagues [34] compared 104 term pregnant women having bishop score < 4 with intravaginal misoprostol and Foley catheter for induction of labor. There were no differences in neonatal outcome in both groups. Misoprostol had shorter induction to delivery time

and higher vaginal delivery rate in cases of unfavorable cervix than Foley catheter but uterine hyper-stimulation was more common in misoprostol group. Fitzpatrick et al [35] conducted randomized trial in 116 low risk women comparing Foley catheter combined with a fixed versus incremental low dose oxytocin infusion. They found no differences between two groups in induction to delivery time, uterine hyper-stimulation, fetal heart rate abnormalities and mode of delivery. Overall, Foley catheter when compared with oxytocin alone is associated with a decreased risk of CS but when compared with prostaglandin shows no differences [36].

Foley or single balloon catheter is an effective method for induction of labor. It is stable at room temperature, easy to store, inexpensive, had low risk of hyperstimulation and can be removed easily if such cases occur but it requires trained personal and patient discomfort. Generally, Foley catheter insertion is avoided in premature rupture of membrane, chorioamnionitis and unexplained vaginal bleeding.

Pharmacological methods

Mechanism and its effects

Since 1960s, prostaglandins have been used for cervical ripening to improve the chances of successful labor induction [37]. Prostaglandins when used as labor induction agents causes activation of collagenase, prompts remodeling of the extracellular matrix, generates uterine contractions, and may initiate labor [38]. Misoprostol is a synthetic PGE1 analog. Misoprostol, used for the treatment of NSAID induced peptic ulcer previously, was approved by US-FDA but it has not been approved yet by FDA for pregnancy. It is available as a oral tablet form and since 1980s it has been used off label for cervical ripening and induction of labor in oral, vaginal and sublingual form [39,40,41,42]. Dinoprostone is a synthetic PGE2 analog which includes cervical gel (2.5 ml syringe with 0.5 mg of active drug), vaginal tablet, and vaginal insert (10 mg of active drug released at a rate of 03 mg/hour) and are administered locally within the reproductive tract. Advantages of PGE1 over PGE2 include its availability, cost effectiveness and stable at room temperature. Difficulty in producing the exact dosing, as the tablet cannot be broken accurately and difficulty in discontinuing the drug in case of hyperstimulation and abnormal fetal heart rate tracing are the main drawbacks of PGE1.

Newer drug delivery system: Misoprostol vaginal insert

The proven efficacy of misoprostol and its drawback had led to the development of the newer drug delivery system, misoprostol vaginal insert (MVI). MVI has been studied in phase II and III clinical trials and will be soon under FDA review [43,44]. Wing et al [44] in his phase II randomized controlled trial compared 3 doses of MVI for labor induction. 374 women with singleton, term, cephalic gestation with bishop ≤ 4 were randomly given 100 μg , 150 μg , and 200 μg MVI which was placed in posterior vaginal fornix and removed if women underwent into active phase of labor or if hyperstimulation sets in or after 24 hours of insertion. The result showed that MVI 200 μg group had shorter induction to delivery time, less need of oxytocin augmentation but higher rate of hyperstimulation than MVI 100 μg group. But CS rate was not statistically different among these groups. Wing et al [45] in his phase III multicenter randomized study compared 1358 women with bishop score ≤ 4 to receive either 200 μg MVI or 10 mg dinoprostone vaginal insert (DVI). MVI group had significantly reduced induction to delivery time, reduced time to active labor and reduced need for oxytocin compared with DVI group. There were no significant differences in case of CS in both groups. Tachysystole was more common in MVI group than in DVI group.

Comparison between pharmacological methods

Taher et al [46] performed Randomized trials in 165 term pregnant women comparing PGE2 vaginal gel and vaginal tablets for induction of labor. Induction to delivery rate and failed induction was higher in vaginal tablets groups than in vaginal gel groups. There was no significant difference between oxytocin uses, uterine hyperstimulation, meconium stained liquor, delivery with CS and adverse maternal and neonatal outcomes showing vaginal gel to be better. Another randomized controlled trial performed by Maria and group [47] studied 133 singleton, cephalic presentation, term pregnant women with bishop ≤ 4 , intact membrane and had no previous CS for induction of labor with either 24 hour controlled release vaginal dinoprostone pessary or vaginal dinoprostone gel. It showed higher rate of spontaneous vaginal delivery in the pessary group and higher rate of operative vaginal delivery in the gel group but there was no statistical significant difference in primary CS rate. Thus, it showed vaginal dinoprostone pessary to be superior.

In a randomized trial conducted by Wilkinson et al [48], 827 women with uncomplicated term pregnancy were randomly selected for either outpatient or inpatient PGE2 for cervical ripening. Fetal heart sound was monitored using Cardiotocography(CTG) before and after PGE2 administration in all women. Oxytocin use, primary CS, Vaginal delivery with 24 hrs and epidural use was similar in both groups. No any clinical advantages or disadvantages were found from this study and uterine hyperstimulation cause by PGE2 leads to failure to use PGE2 as outpatient tool. A meta-analysis comparing cervical ripening agents like dinoprostone gel and dinoprostone insert reported that rate of vaginal delivery within 24 hours, shorter hospital stay and less postpartum hemorrhage was increased in dinoprostone insert, but insert was not as effective as gel in altering the rates of Vaginal delivery in women with intact membrane and an unfavorable cervix, assisted vaginal delivery or primary CS [49,50].

In a study done by Sayeda and colleagues in Pakistan, 249 term low risk pregnant women with bishop score ≤ 6 were induced with vaginal misoprostol and vaginal PGE2. Primary CS risk, the mean induction to delivery time and the Apgar score were similar in both groups. The vaginal misoprostol, though cheaper than PGE2, showed higher NICU admission [51]. Another meta-analysis of 280 randomized trials concluded that among all prostaglandins, misoprostol may be the best for labor induction. Titrated low dose oral misoprostol appeared to be safe for primary CS whereas vaginal misoprostol for achieving vaginal delivery within 24 hours [52].

A multicenter prospective randomized study in china analyzed 173 nulliparos term women with bishop score ≤ 6 for cervical ripening and induction with 25 μg intravaginal misoprostol. This study showed increased rate of vaginal delivery within 24 hours and shorter length of induction to onset of labor in misoprostol group than in placebo group. No significant differences were found in CS rate, maternal and neonatal outcomes between two groups [53]. In Azubuike et al [54] study, 88 postdated nulliparous women with bishop score ≤ 5 were randomly selected for either 25 μg or 50 μg intravaginal misoprostol for induction of labor. No differences in case of induction to delivery time, need of augmentation, CS, uterine hyperstimulation was found in two groups. But side effect of misoprostol like vomiting was increased with its increasing dose leaving low dose misoprostol to be effective and safer.

In a randomized controlled trial [55], 126 low risk nulliparous women with unfavorable cervix (bishop score ≤ 4) were randomly selected to receive 25 μg sublingual misoprostol with vaginal placebo and 50 μg intravaginal misoprostol with sublingual placebo. No significant differences were found between two groups in regard to induction to delivery time, vaginal delivery within 12 hours, rate of hyperstimulation, types of delivery, cause of CS, and neonatal outcomes. Here, low dose of sublingual misoprostol was found to be more effective than vaginal misoprostol for cervical ripening and induction of labor. Another randomized study [56] of 140 women was compared with 25 μg sublingual and 25 μg vaginal misoprostol for cervical ripening and induction. No significant differences were seen in both groups regarding mode of delivery, maternal and neonatal outcomes. Fetal distress and non-progress of labor was the main indication for CS in both groups.

Conclusion

As the rate of induction of labor continues to increase, the choice should be made to improve and develop more effective and rapid method of induction that can cut short the induction to delivery time maintaining maternal and neonatal safety. There are several methods of labor induction but no single agent seems to be superior to others. When comparing misoprostol (PGE1) with vaginal dinoprostone (PGE2), we found that there were decreased rate of CS with misoprostol. But it was related with increased uterine hyperstimulation. Uterine hyperstimulation was comparatively low with mechanical methods than with pharmacological methods of induction. Due to its low cost, lower rates of uterine hyperstimulation and relatively safe than other induction method, mechanical method especially intravaginal Foley catheter can be an effective agent in developing countries. Further research may be necessary to identify the benefits and risks of methods of labor induction.

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