



TO COMPARE CERVIX RIPENING (USING MODIFIED BISHOP SCORE) BETWEEN PROSTIN E2 AND LAMINARIA + PROSTIN E2 IN WOMEN UNDERGOING INDUCTION OF LABOUR

Dr Hina Mushtaq^{1*}, Dr Sana Ghaffar Bajwa², Dr Nida Arif³, Dr Sobia Haneef⁴, Dr Komal Tariq⁵, Dr Lubna Bibi⁶

^{1*,2,3}Post Graduate Resident Gynae & Obs, MCH Unit 2; PIMS Islamabad, Pakistan

⁴Post Graduate Resident Pediatrics Medicine, Children Hospital; PIMS Islamabad, Pakistan

⁵Post Graduate Resident Cardiology, Ayub Teaching Hospital, Abbottabad, Pakistan

⁶Post Graduate Resident Gyne & Obs, HMC Hospital, Peshawar, Pakistan

***Corresponding Author:** Dr Hina Mushtaq

*Post Graduate Resident Gynae/Obs, MCH Unit 2; PIMS Islamabad

E-mail address: dr.ham9187@gmail.com

ABSTRACT

Objectives: To compare cervix ripening between laminaria+Prostin E2 and Prostin E2 alone in women undergoing induction of labour.

Study design: Randomized controlled trial.

Place and duration of study: This study was conducted at the MCH Center, Unit-II, Pakistan Institute of Medical Sciences, Islamabad from 1st of November 2020 to 30th of April 2021. **Methods:** A total of 132 pregnant women with 37-42 weeks of gestation having singleton pregnancy and planned for induction of labour with unfavorable cervix (bishop score <5) were enrolled in this study and divided in 2 equal groups. In Group A, patients were inserted laminaria tents and intravaginal Prostin E2 3mg tablet (dinoprostone) while in-group B women only received intravaginal Prostin E2 3mg tablet. Primary outcome was set as improvement in modified bishop score and number of women where cervix ripening was achieved. The secondary outcomes were rate of spontaneous vaginal delivery, cesarean section and fetal wellbeing.

Results: The Mean±SD of age in this study was 27±4.6 years. The results of primary outcomes of study showed that women in Group A achieved significantly higher modified bishop score compared to women in Group B (8.9 ± 0.74 Vs 8.1 ± 0.33 , respectively, $p=0.000$). Similarly, cervix ripening was achieved in significantly more women in Group A compared to Group B (68.2% Vs 43.9% respectively, $p=0.005$). The results of secondary outcomes showed that significantly more women had spontaneous vaginal delivery, lesser needed caesarean section and neonates had significantly better APGAR score at 1 minute in Group A compared to Group B. **Conclusions:** The administration of laminaria along with Prostin E2 tablets results in higher modified bishop score indicating better cervix ripening than Prostin E2 tablets alone in women undergoing induction of labour.

KEY WORDS: Cervix ripening, Induction of labour, Laminaria, Modified bishop score, Prostin E2.

Introduction:

Requirement of induction of labour (IOL) in the third trimester is in routine to cover the possible associated risks to the mother and the fetus. For proper labour induction, cervical ripening is the base, as unripen cervix can cause induction failure, prolonged labour or instrumental delivery. IOL is indicated in the third trimester, when further continuation of pregnancy could have risks for the fetus or the mother.¹ In this scenario, strategies to achieve the cervix ripening become important for a successful procedure of induction.^{1,2}

Over the last two decades, the incidence of labour induction has gradually inflated. Its indication is variable due to a medical condition like gestational diabetes, eclampsia or any obstetrical complication. There is also a trend of on request induction or even selecting induction for nonmedical/social reasons. When the doctor declares that a labor induction is required, selecting the best IOL technique for a given situation is the next step. A number of factors may impact the selection of method for induction, such as the status of cervix and the membrane, patient, parity and the choice of health care provider.³

The success of IOL is based on cervical ripening which is measured by bishop score in later stages of pregnancy. Bishop score is found to have clear advantages for determining preinduction cervical ripening, when compared to other techniques like transvaginal ultrasonography and vaginal fetal fibronectin.⁴

For induction of labor in cases of unfavorable cervix, prostaglandin analogs represent the most commonly used pharmacological approach. Prostaglandin E2 (PGE2) has dual effects of promoting cervical ripening and stimulating uterine contractions, making it an effective agent for initiating labor. Importantly, PGE2 exhibits relatively minimal negative effects compared to other methods. Dinoprostone is the prostaglandin analog available with the commercial name of Prostin E2 specifically formulated and developed for facilitating cervical ripening and preparing the cervix for labor induction. It is available in the forms of gel preparation, vaginal suppository insert and vaginal tablets allowing the localized delivery of PGE2 to the cervical tissues, enabling efficient ripening. In Pakistan, it is available in the form of 3mg vaginal tablets.^{5,6,7}

For the mechanical approach of cervical ripening, osmotic dilation conducted by using laminaria is an effective method. Laminaria tents are made from natural sea plant laminaria hyperborean. They are intensively hygroscopic when placed in tissue and swell 3 – 5 times their initial diameter in 6 – 8 hours. The process cause an enlarged diameter when laminaria is inserted into the cervical canal leading the cervix to gradually stretch. Another mechanism by which these devices may induce uterine contractions is through stimulation of the Ferguson reflex. Laminaria were used many years ago to dilate the uterine cervix but discontinued due to unsatisfactory sterilization and resultant uterine infection. However, recently, adequate sterilized laminaria tents have been shown to be safe and effective in increasing the inducibility of the unripe cervix at or near term.^{5,8,9,10}

The purpose of this study was therefore to compare the cervix ripening between Prostin E2 complemented by laminaria and Prostin E2 alone in women undergoing induction of labour. These results help the health care providers to select the evidence base methods for induction of labour in our local health care set ups.

Methodology:

This randomized control trial was conducted at the MCH Center, Unit-II, Pakistan Institute of Medical Sciences, Islamabad from 1st of November 2020 to 30th of April 2021 over a period of 6 months.

The sample size was calculated with following assumptions:

Mean bishop score in Prostin E2 group= 3.8 ± 1.46

Mean bishop score in laminaria+ Prostin E2 group= 5.1 ± 2.7 .¹¹ With confidence interval=95% and margin of error=5% , the estimated sample size: $n_1=66$, $n_2=66$.

A total of 132 women in 37-42 weeks of gestation with unfavorable cervix (bishop score <5), having singleton pregnancy and planned for induction of labour due to hypertension, gestational DM, post maturity and poor obstetrics were added in this study using consecutive sampling.

Women were randomized in 2 equal groups of 66 patients each by employing lottery method.

Exclusion criteria was set as women with known type II diabetes mellitus, severely malnourished, dead fetus in womb, preeclampsia and vaginal infection were excluded.

In Group A, patients were inserted laminaria tents and intravaginal Prostin E2 3mg tablet (dinoprostone) while in-group B women only received intravaginal Prostin E2 3mg tablet. On the day of procedure bishop score was evaluated and only those with a score of less than 5 qualified for the study. The vagina was cleansed with pyodine solution, a Cusco's bivalve speculum introduced and the cervix was visualized.

In Group A, 12 hours before the planned IOL, the anterior lip kept steady with a spogne-holding forceps and 2 or 3 laminaria tents introduced beyond the internal OS, using another sponge holding forceps. The tents kept in position with a sterile vaginal tampon. Prostin E2 tablet was inserted with the help of a pill applicator 6 hours prior to plan IOL.

In Group B, Prostin E2 tablet was inserted with the help of a pill applicator 6 hours prior to plan IOL. Primary outcome was set as improvement in modified bishop score and number of women where cervix ripening (bishop score ≥ 8) was achieved. The secondary outcomes were rate of spontaneous vaginal delivery (SVD), cesarean section (CS) and fetal well-being.

A written consent was taken from women for participation in the study.

Approval of conducting the study was taken from ethical committee of the hospital. Data analysis was performed using SPSS version 25. Quantitative variables were presented in shape of mean and standard deviation while qualitative variables were expressed in form of frequency and percentage. Independent samples t-test and Chi-square test was used to compare the outcomes between the groups. A p-value of < 0.05 was considered significant.

Results:

The Mean \pm SD of age in this study was 27 \pm 4.6 years with an age range from 18 to 36 years. The details of demographics and medical history are given in Table-I.

Table-I: Demographics and medical history.
n=132

Demographics and medical history	Group A (n=66)	Group B (n=66)
Age (Mean \pm SD) years	26.7 \pm 4.59	27.3 \pm 4.64
BMI (Mean \pm SD) kg/m ²	26.46 \pm 2.4	26.92 \pm 3.81
Gestational age (Mean \pm SD) weeks	38.9 \pm 1.11	39.08 \pm 1.21
Gravida (Mean \pm SD)	2.29 \pm 0.77	2.22 \pm 0.77
Parity (Mean \pm SD)	1.64 \pm 1.09	1.63 \pm 1.05
Baseline Bishop score (Mean \pm SD)	2.61 \pm 0.7	2.5 \pm 0.71

At the time of induction the mean modified bishop score was significantly higher in Group A compared to Group B. Similarly, higher proportion of women demonstrated cervix ripening in Group A compared to Group B as shown in Table-II.

Table-2: Study outcomes n=132

Study outcomes	Group A (n=66)	Group B (n=66)	p-value
Modified bishop score (Mean \pm SD)	8.9 \pm 0.74	8.1 \pm 0.33	0.000
Patients achieving cervix ripening n (%)	45 (68.2)	29 (43.9)	0.005
SVD n (%)	38 (57.6)	26 (39.4)	0.037
Patients needing CS n (%)	8 (12.1)	21 (31.8)	0.006

The neonatal outcomes of the study show a better APGAR score at 1 min. in Group A compared to Group B. However, no significant difference was present among the groups regarding APGAR score at 5 minutes, birth weight and NICU admission rate as shown in Table-III.

Table-III: Neonatal outcomes n=132

Neonatal outcomes	Group A (n=66)	Group B (n=66)	p-value
Apgar score at 1 min (Mean±SD)	7.2±0.84	6.4± 1.1	0.000
Apgar score at 5 min (Mean±SD)	7.8±1.1	7.6±1.3	0.368
Birth weight (Mean±SD) gm	2984.7± 377.7	2981.4±404.5	0.986
NICU Admission n (%)	21 (31.8)	25 (37.9)	0.465

Discussions:

The cervical ripening method is chosen based on effectiveness, safety profile, and the medical/obstetric history of the patient. There are different pharmacological approaches and mechanical techniques to prepare the cervix for induction in cases of term pregnancies. However, no single method is considered the best for cervical ripening in cases of term pregnancies. Mechanical methods are found to be effective for initiating labor, and combining them with other induction techniques can yield optimal outcomes.^{12,13}

Prostin E2 and laminaria are discussed as combination in very few studies, however, a lot of studies have discussed the effectiveness of Prostin E2 and laminaria alone or in combination with other pharmacological agents.

Agarwal K compared the pharmacologic strategies of Prostin E2 with isosorbide mononitrate to find the cervix ripening in women at term admitted in hospital with bishop score ≤ 6 . The results showed significantly better cervical ripening as assessed through higher bishop score in Prostin E 2 group and lesser time from the start of pharmacologic intervention to SVT. However, there were concerns of uterine tachysystole events in Prostin E2 group compared to the other group.¹⁴ Behnoud F compared the results of misoprostol alone and in combination with laminaria. The study outcomes were in favor of the combination where duration of labor, use of curettage and length of hospital stay were reduced compared to misoprostol alone.¹⁵

Sheikham S compared the combination of misoprostol and laminaria with the combination of misoprostol and letrozole and concluded that combination of misoprostol and laminaria is more effective than the other combination.¹⁶

Behrashi M compared the outcomes in at term women administered with misoprostol (25 μ g/vaginal) and a single dose of laminaria intracervically. The induction time to the active phase of labor and the induction time to delivery did not significantly differ between the two groups. Compared to the laminaria group, the misoprostol group had a higher cesarean frequency rate (P=0.017). The study concluded that for cervical ripening, laminaria appears to be more safe and effective than misoprostol, they however, asked for studies with larger sample sizes and additional research for more conclusive outcomes.¹⁷

In a study by Heydari A, a comparison was made between misoprostol (a prostaglandin E1 analog that is commonly used for cervical ripening and labor induction) and laminaria. The researchers reported that after the drug administration, the changes in cervical dilation was 4.4 times more in laminaria group compared to group taking misoprostol (p=0.001). The rate of CS was also reported to be significantly higher in misoprostol group compared to laminaria group (p=0.017). However, during the labor, misoprostol group was better regarding rate of oxytocin administration than the group where laminaria was used (p=0.0001).¹⁸

In a systematic review, de Vaan et al. assessed clinical studies that compared pharmaceutical and mechanical approaches of cervical ripening for labor induction at third trimester. A total of 113 randomized controlled studies including 22,373 women who had various reasons for being scheduled for labor induction were included in this review. There were 8 studies comparing laminaria tent plus vaginal PGE2 versus PGE2 alone for cervical ripening/induction of labor. The results shared that a

greater proportion of women (74.6% versus 51.8%) showed signs of cervix ripening 24 hours after the intervention. Moreover, better SVD rate was observed with this intervention in laminaria+PGE2 group compared to PGE2 alone group (41.9% Vs 29.4%). The rate of CS was also lower in the combination group compared to PGE2 alone in the pooled results of this analysis (39.1% Vs 33.6%).⁹

The Mean±SD of age in our study was 27±4.6 years with an age range of 18-36 years. The results of primary outcomes of study showed that women in Group A achieved significantly higher modified bishop score compared to women in Group B (8.9 ± 0.74 Vs 8.1 ± 0.33 , respectively, $p=0.000$). Similarly, cervix ripening was achieved in significantly more women in Group A compared to Group B (68.2% Vs 43.9% respectively, $p=0.005$). The results of secondary outcomes showed that significantly more women had SVD, lesser needed CS while neonates had significantly better APGAR score at 1 minute in Group A compared to Group B. These results are in line with the results shared for Prostin E2, laminaria alone or in combination for women at term undergoing IOL and provide further evidence of using the strategy of combining these mechanical and pharmacological techniques.^{11,13,14,15,16,17,18}

In short, we can say that mechanical induction techniques are useful since they may offer a higher level of safety than pharmacological techniques, but this may be at a cost of more labor. These considerations of combining these 2 methods must be taken into account in order to choose the most effective procedures based on the clinical circumstances.

The major limitation of our study is that we worked on most important but only selected parameters for evaluating the success of this induction technique. Future studies working on broader range of assessment tools will be help in adding up in this useful data.

Conclusions:

The benefits of this Laminaria+ Prostin E2 combination appears in shape of higher modified bishop score, providing better cervix ripening than Prostin E2 tables alone in women undergoing IOL. The administration of this strategy may provide a good management option in women at term and undergoing IOL due to certain reasons in our health care set ups.

Disclaimer:

No

Conflict of interest:

No

Acknowledgements:

The services of paramedical staff of our unit for their help in taking and maintaining patient's data are acknowledged.

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