

How to Cite:

Nivethitha, S. K., & Jeyamani, B. (2022). A prospective randomized comparative study between Sustained release vaginal insert and intracervical gel in women with unfavourable cervix at term pregnancy. *International Journal of Health Sciences*, 6(S6), 3839–3846. <https://doi.org/10.53730/ijhs.v6nS6.11524>

A prospective randomized comparative study between Sustained release vaginal insert and intracervical gel in women with unfavourable cervix at term pregnancy

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Abstract---Background-Induction of Labour (artificially initiated labour) is a common obstetric practice in pregnant women throughout the world, accounting for 20% of all births. Induction of Labour should be performed only when there is a clear medical indication for it and the expected benefits outweigh its potential harms. Objectives- to compare between the two formulations of dinoprostone and study the better option among the two, in cervical ripening and labour induction in women with unfavourable cervix. Methods- It was a Prospective randomized comparative study done in total 100 consecutive term pregnant women who underwent labor induction for fetal or maternal indications were divided randomly into two groups. Group A - sustained release vaginal insert and Group B - Intracervical gel. Informed consent was taken from each patient. SPSS (Version 22.0) was used for analysis. Results- Statistically significant increase in final Bishop's score ($p=0.01$) and hyperstimulation ($p=0.04$) was seen in Vaginal insert group as compared to Intracervical gel group, while there were no statistically significant differences in maternal outcomes, neonatal outcomes and need for oxytocin augmentation in both groups. Conclusions- We found that insert did not improve the induction delivery interval or rate of successful induction, nor did it have any advantage in terms of neonatal outcome although it did improve the Bishop's score – Its advantage was in terms of single

application, few prevaginal examinations, longer duration of action and immediate retrieval in case of hyperstimulation.

Keywords---labour, bishop score, hyperstimulation, dinoprostone, intracervical gel, apgar score.

Introduction

Induction of Labour (artificially initiated labour) is a common obstetric practice in pregnant women throughout the world, accounting for 20% of all births. Induction of Labour should be performed only when there is a clear medical indication for it and the expected benefits outweigh its potential harms.[1] BISHOP'S SCORE is a simplified scoring system based on digital cervical examination of a patient that takes into account, cervical effacement, dilatation, station which are scored 0-3 points while cervical position and consistency are scored 0-2 points. The Bishop's score is used to determine whether or not the cervix is 'favourable' and to assess whether or not cervical ripening is needed. Low Bishop's score leads to higher incidence of prolonged labour and caesarean section.[2,3]. If a cervix is favourable, labour induction is normally undertaken with oxytocin and/or amniotomy. If a cervix is considered to be unfavourable, no method is highly effective for induction so that patient is a candidate for cervical ripening. Cervical ripening is a process that helps the cervix to prepare for labour and can result in a more favourable cervix. The two main methods of cervical ripening are prostaglandin use and mechanical method. Prostaglandins can be given vaginally, buccally, or orally to a patient with an unscarred uterus that can help to achieve a more favourable Bishop score in 12 to 24 hours. FDA approved dinoprostone vaginal insert in 1995 for cervical ripening.[3,4]

Propess

A sustained release dinoprostone vaginal insert should remain sealed in the foil sachet and stored in a freezer (-10 to -25°C)- removed from the freezer just prior to insertion. After opening, the pessary is held between the index and middle finger and is positioned transversely high in the posterior fornix using only small amount of water soluble lubricants. The patient should be recumbent for 20-30 minutes after insertion. As dinoprostone will be continuously released over a 24 hour period at the rate of 0.3mg/hour, it is important to monitor uterine contractions and fetal condition at regular intervals. Furthermore, because of the integral retrieval system, Dinoprostone vaginal insert can be easily and quickly removed at the end of the 24-hour dosing period or once the onset of active labour has begun or in case of hyperstimulation.[5,6]

Cerviprime

Is a Dinoprostone gel 0.5 mg available in a 2.5 ml disposable syringe with a catheter. It should be stored in refrigerator between 2- 80 C. With the women in supine position, tip of the prefilled syringe is placed intra-cervically and the gel is kept just below the internal os. Maximum of 3 doses may be repeated every 6

hours recommended in 24 hours. Being a gel inserted intracervically, retrieval is not possible.[6]

Materials and Methods

It was a Prospective randomized Comparative study done after obtaining ethical clearance and informed consent from the patients, study was conducted in the Department of Obstetrics and Gynaecology, VMKV Medical college and Hospital, Salem. Between March 2022 - August 2022. Pregnant women with gestational age more than 37 weeks attending obstetrics OPD of Vinayaka Mission's KirupanandaVariyar Medical College and Hospital, Salem were the study population found to be 100 which was the sample size.

Inclusion Criteria

- Primigravida / multigravida with previous normal delivery
- Singleton pregnancy
- Cephalic presentation
- Gestational age > 37 weeks
- Bishop's score less than or equal to 6 with intact membranes
- Maternal age >19 years and < 35 years
- Reactive fetal Non-stress test
- Medical / obstetric indication for induction
- Booked cases

Exclusion Criteria

- Previous caesarean delivery
- Pregnant women with previous history of uterine surgery
- Preterm gestation
- Multiple pregnancy
- Fetal mal-presentation
- Cephalopelvic disproportion
- Suspicion /evidence of fetal distress
- History of bronchial asthma
- Placenta previa / unexplained vaginal bleeding
- Current Pelvic Inflammatory Disease

Methodology

This was Prospective randomized comparative study including 100 pregnant women who underwent labor induction for fetal or maternal indications in our institute including all emergency as well as registered cases. In this study two types of prostaglandin formulations – intra cervical PGE2 gel and PGE2 sustained release vaginal pessary are used in cervical ripening and labour induction. Each patient were asked for detailed history. A careful general physical examination and systemic examination was carried out in all the patients. The information pertaining to the study like fundal height, fetal presentation, engagement, uterine contractions fetal heart sound, effacement and dilatation of cervix, presence of

bag of membrane, station of the presenting part, and adequacy of pelvis was noted. All routine and specific investigations was done.

A comparative study of two groups, "Group A" – induced with sustained release dinoprostone vaginal insert and "Group B" – induced with intracervical dinoprostone gel. CTG trace was taken for up to 30 minutes immediately after induction in both the groups followed by intermittent CTG monitoring every 4th hourly. Uterine contractions, baseline fetal heart rate, variability, accelerations and decelerations to be recorded. Once when active labour has begun or in case of uterine hyperstimulation or in evidence of fetal distress, it is necessary to remove the vaginal delivery system to terminate drug administration. Induction delivery interval, maternal outcomes in terms of normal vaginal delivery, instrumental vaginal delivery or caesarean sections and neonatal outcomes in terms of meconium stained liquor, APGAR score and NICU admissions was recorded. Successful induction or ripening is defined as bishops score between 7-9 (>3 cm dilated and 60-70% effaced) at the end of 24 hours in both the groups. When Bishop's score is still less than or equal to 6 at the end of 24 hours from the beginning of induction then it is stated as failed induction.

Statistical Analysis

Statistical analysis was performed by using Statistical Package for Social Sciences (SPSS) version 22.0 (SPSS Inc., Chicago, IL, USA). Independent sample t-test was used to compare quantitative between two groups. Fisher's exact test was used to compare number qualitative variables reported between the two groups. $P < 0.05$ was considered statistically significant.

Results

Table 1
Final Bishop's scoring

Final bishop's score	Sustained Vaginal Insert	Intracervical Gel	p-value
0-6	19(38)	20(40)	0.81
7-9	18(36)	8(16)	0.01*
≥10	13(26)	22(44)	0.13

As per table 1 statistically significant difference was found between twogroups in final Bishops score of 7-9 range group (p value= 0.01).

Table 2
Maternal Outcomes in study participant

Maternal Outcomes	Sustained Vaginal insert (A)	Intracervical Gel(B)	p-value
NVD	15(30)	17(34)	0.51
Vaccum delivery	2(4)	3(6)	0.81
LSCS	12(24)	10(20)	0.41

Forceps delivery	2(4)	0(0)	0.37
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As per table 2 Successful maternal outcomes were considered only in women who achieved cervical ripening with Dinoprostone (either vaginal insert or intracervical gel). A total of 31 women in vaginal insert group achieved successful cervical ripening (Bishops score was >7) out of which 17 delivered normally or had assisted instrumental vaginal delivery. The remaining 12 in vaginal insert group delivered by caesarean section. Whereas in intracervical gel group 30 pregnant women achieved successful cervical ripening out of which 17 women delivered normally or assisted vaginal delivery and 10 were delivered by caesarean section. However maternal outcomes were compared between two groups, there was no statistically significant difference observed when statistical analysis was done (p value > 0.05 using student t-test).

Table 3
Incidence of Hyperstimulation and Meconium stained liquor

Hyperstimulation and Meconium stained liquor	Sustained Vaginal insert	Intracervical Gel	p-value
BS≤6	3(6)	0(0)	0.01*
BS≥10	4(8)	3(6)	0.25
MSL	6(12)	2(4)	0.41

As per table 3 Hyperstimulation was observed in 7 out of 50 pregnant women in vaginal insert group. Bishops score was assessed at the time of removal of vaginal insert. It was ≤6 in 3 out of 8 women and ≥10 in 4 out of 7 women. Whereas hyperstimulation was seen in only 3 out of 50 women in intracervical gel group. Both these patients had Bishops score ≥10. More women in the insert group had hyperstimulation and this finding was statistically significant (p value 0.01). Meconium stained liquor was noted in 6 women out of 50 women in vaginal insert group and 2 out of 50 women in intracervical gel group. However, this difference was not statistically significant.

Table 4
Comparison of induction delivery interval in both groups

Parameters	Sustained Vaginal insert	Intracervical Gel	p-value
Within 12 hours	0(0)	0(0)	1
12-24 hours	5(10)	4(8)	0.50
≥24 hours	13(26)	17(34)	0.37

As per table 4 induction delivery interval was calculated in women who delivered normally. In both the groups none of the women delivered within 12 hours of induction. In vaginal insert group, 18 pregnant women delivered normally and induction delivery interval was between 12-24 hours in 5 and more than 24 hours in remaining 13 women. In intracervical gel group, 21 pregnant women delivered normally and induction delivery interval was between 12- 24 hours in 4 and more than 24 hours in remaining 17 pregnant women. Even though induction delivery

interval was shorter in vaginal insert group, no statistically significant difference was seen.

Table 5
Indication of LSCS in study participants

Indication	Sustained Vaginal insert	Intracervical Gel	p-value
Fetal distress	8(16)	6(12)	0.41
MSL	5(10)	3(6)	0.50

As per table 5 eight out of 13 delivered by caesarean section in vaginal insert group due to fetal distress and the rest 5 women underwent caesarean section due to meconium stained liquor with unfavourable Bishop's score. Nine women in intracervical gel group delivered by caesarean section out of which 6 women underwent caesarean section due to fetal distress and 3 women underwent caesarean section due to meconium stained liquor with unfavorable Bishop's score. No statistically significant difference was found between two groups.

Table 6
Comparison of Neonatal Outcomes in both groups

Outcome	Sustained Vaginal insert	Intracervical Gel	p-value
Apgar score in 1 min and 5 min <7	3(6)	4(8)	0.43
NICU admission >24 hours	8(16)	5(10)	0.58

As per table 6 Neonatal outcomes were compared only in neonates of women who delivered vaginally with either vaginal insert or intracervical gel. Apgar score <7 was noted in 3 out of 31 neonates in vaginal insert group and 4 out of 30 neonates in intracervical gel group. 8 out of 31 neonates in vaginal insert group needed NICU admission for >24 hours and 5 out of 30 neonates in intracervical gel group needed NICU admission >24 hours. When neonatal outcomes were compared no statistically significant difference was found between both groups

Discussion

The success of induction depends upon the condition of cervix. Unfavorable cervix leads to failure of induction and increases the chances of delivering by caesarean section. In the present study the effectiveness of intracervical gel and vaginal insert in primiparous women was compared by taking initial bishops score of ≤ 6 as inclusion criteria. Various other studies have taken Bishops score as ≤ 6 Mukhopadhyay et al, ≤ 8 Ottinger et al, ≤ 4 Fabio fachinetti et al.[7,8,9] All mentioned studies included primiparous women to compare vaginal insert and intracervical gel which was similar to this study. Westgate J et al, and Trofatter KF et al, had outcomes similar to this study whereas Fachinetti F et al, Annamaria et al, compared the cervical ripening efficacy of both Dinoprostone preparations and concluded that intracervical gel was more effective than vaginal pessary in achieving cervical ripening.[9,10,11] Most of the abovementioned studies included both primi and multigravidae and used vaginal insert only for 12 hours. Whereas

the current study used vaginal insert for 24 hours and included only primiparous women. Mazouni et al, using vaginal pessary, found that pregnant women had a 3.5 fold higher risk of caesarean section.[12] Pevzner L et al, evaluated cardiotocographic abnormalities associated with Dinoprostone vaginal insert and noticed 35% delivered by caesarean section due to CTG abnormalities with vaginal insert.[13]

In the present study no pregnant women delivered neonate with Apgar <7 at 5 min in both groups and this was consistent with the findings of Vollebregt et al, Strobelt et al and El-shawarby et al.[14,15,16] In vaginal insert group 14% neonates required NICU admission for more than 24 hours in this study whereas in gel group 12% required NICU admission for >24 hours. In a study by Rugarn O et al, only 3.7% of neonates had NICU admissions with vaginal insert.[17] In this study little higher incidence of meconium stained liquor seen in vaginal insert group (12% versus 4%). Rugarn O et al, found meconium stained liquor in 18.5%.[17]

Conclusion

Sustained release vaginal insert had an advantage of metered release of Dinoprostone and there was statistically significant improvement in bishops score in range of 7-9 but it did not translate into successful induction. Advantage with vaginal insert was immediate retrieval system especially in case of hyperstimulation. Vaginal insert did not prove to be better than intracervical gel on the whole when overall outcome of induction was considered.

Author's Funding- None

Conflict of Interest- None declared

Author's Contribution

Dr. A has finalized the draft and guarantor, Dr. B and C has prepared the conceptual framework, designing of draft, and data analysis, Dr. D was involved in data collection and analysis, and Dr. E has done manuscript writing and data collection.

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