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A Study On Safety And Effectiveness Of Endocervical Application Of Dinoprostone Gel For Induction Of Labour At Term And Pharmacoeconomic Analysis Of Various Brands Of Dinoprostone Gel

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ABSTRACT: The main objective of the study is to determine whether the endocervical application of dinoprostone gel is safe to use in pregnant patients to observe the therapeutic effect of Dinoprostone gel. This study gives us the incidence of foeto-maternal outcomes by checking the maternal and neonatal health after successful induction. The study also has the objective to study the pharmaco-economic analysis of various brands of Dinoprostone gel. After designing data collection form and study tools, Patient will be selected based on inclusion and exclusion criteria. We include age, gender, chief complaints, history of present illness, past medication history, obstetric history, lab investigation, abdominal scan report and therapeutic management of the patient and these will be collected using data collection form. Other information like time of administration of dinoprostone, time taken for induction, etc. are also collected by interviewing the patients and other health professionals in the respective ward. The collected data will be analysed using suitable statistical tools**.**

KEYWORDS: Endocervical, Dinoprostone, Pharmacoeconomic Analysis, Neonatal Health

I. INTRODUCTION

The ultimate outcome of good Obstetric care is the delivery of a healthy baby with a healthy mother. A fact that sounds so simple is actually a coveted aim achieved only after meticulous planning of antenatal care and delivery.

Labour is a process through which the foetus moves from the intrauterine to the extrauterine environment. It is a clinical diagnosis defined as the initiation and perpetuation of uterine contractions with the goal of producing progressive cervical effacement and dilatation. When the benefits of delivery outweigh the continuation of pregnancy, there arises the need for "induction of labour".

The main aim of this process is to give birth via vaginal delivery on a successful induction. Induction primarily refers to the attempt to produce regular uterine contractions along with cervical changes to begin the active phase of labour. To be successful, induction of labour must fulfil three aims.

1. First it should result in labour, namely adequate uterine contractions and progressive dilatation of cervix.
2. Second this labour should result in vaginal delivery, as there is little purpose in bringing about labour as a mere preparation for caesarean section.
3. Third, in viable pregnancies, these aims must be achieved with minimum discomfort and risk to both mother and foetus.

II. BACKGROUND OF THE STUDY

Multiple pharmacological, mechanical and complementary methods are available to induce labour. There are various medications used for induction. The ideal agent is one that decreases the time to achieve delivery without compromising maternal or neonatal safety. To induce labour successfully, a good cervical status and favourable obstetrical conditions are necessary. If these

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conditions are not present, cervical ripening must be induced before labour. Intravaginal or intracervical administration of prostaglandin E2 is actually the standard for cervical ripening. The mean Bishop score improved from 3.36 to 7.0 in an average of 2hours and 37 minutes after a preceding intracervical application of 0.1, 0.2 or 0.3mg PGE2 in 1ml viscous gel. The cervical diameter found to be increased and delivery occurred spontaneously. Foetal outcome was normal in all cases, with an average APGAR score of 8.7. This observational study is to determine safety and effectiveness of Dinoprostone gel. Therapeutic effect as well as foeto-maternal outcomes will be studied. The study also compares the favourable and unfavourable conditions during delivery and estimates the ratio between successful and failed induction after application of dinoprostone endocervically.

III. LITERATURE REVIEW

Nuria López-Jiménez et al 2022, **Purpose:** To evaluate the effect and safety of vaginal dinoprostone in pregnant women with PROM who undergo induction of labour (iol). **Materials and Methods**: Prospective observational study conducted at La Mancha Centro hospital from 1 February 2019, to 30 August 2020. Obstetric and neonatal variables of 94 pregnant women with PROM who underwent iol with vaginal dinoprostone were analysed, and the results were compared with 330 patients without PROM who also underwent iol. Bivariate and multivariate analyses were performed using binary and multiple linear regression. **Results:** A total of 424 women were included in this study. A greater response to cervical ripening (Bishop score > 6) with PGE2 was observed in the PROM group (odds ratio (OR) 2.73, 95% confidence interval (CI) 1.50–4.99, p = 0.001), as well as a shorter total duration of iol (mean difference (MD) 2823.37 min (min), 95% CI 1257.30–4389.43, p < 0.001). Caesarean sections were performed in 28.7% (n = 27) of patients in the PROM group vs. 34.2% (n = 113) of patients in the non-PROM group, with no significant differences (OR 0.87%, 95% CI 0.47–1.60, p = 0.652). There were no significant differences in changes in the cardiotocographic record (CTG), postpartum haemorrhage (PPH), uterine rupture, or adverse neonatal outcomes between the two groups. **Conclusions:** The use of vaginal dinoprostone in pregnant women undergoing iol with PROM is safe for the mother and the foetus, shortens the total delivery time, and does not increase the risk of caesarean section compared with pregnant women undergoing iol without PROM.

Nguyen Duy Anh et al 2022, **Background:** Induction of labour (IOL) is a technique to establish vaginal delivery when the risks for continuing the pregnancy for mother or baby are higher than the risks of delivery. It is usually performed in high-risk pregnancies, but can also be beneficial in low-risk populations, as shown in the ARRIVE trial. **Objective:** To evaluate the effectiveness and safety of slow-release vaginal dinoprostone (prostaglandin E2 10 mg) for labour induction in women with low-risk pregnancies. **Methods:** A prospective study was performed at Hanoi Obstetrics and Gynaecology Hospital, Vietnam. We recruited women with low-risk pregnancies from 39 weeks + 0 days to 40 weeks + 6 days of gestation and an unfavourable cervix. Women who participated received 10 mg intravaginal slow-release dinoprostone (Propess) for induction of labour. Labour, deliveries, and post-partum management were performed according to the local protocol. Results: From September 2020 to March 2021, 102 low-risk women were eligible to participate in the study. Among these women, 67.6% had vaginal deliveries, 6.9% had postpartum bleeding, and 3.9% experienced tachysystole. All new-borns were healthy, with good APGAR scores. None of the women needed respiratory support or intensive care unit admission. All other maternal or foetal complications were explored. The rate of caesarean section was 3.8 higher in nulliparous than multiparous women and 2.2 times higher in women who did not receive epidural analgesia than in those who did. The risk of caesarean section increased if the time between labour induction and active labour was greater than 12.5 hours. **Conclusion:** Slow-release dinoprostone insert is safe and effective for the 31 induction of labour in low-risk pregnant women. The risk of caesarean section was elevated in nulliparous patients and those who did not receive epidural analgesia during labour. As the time from labour induction to active labour increased, the risk of caesarean section increased.

Anju Bhatia et al 2021, **Aim:** To compare the efficacy and safety of dinoprostone vaginal insert (DVI) alone versus DVI with adjunctive sweeping of membranes (ASM) for induction of labour (IOL). **Methods:** Single-centre, prospective, randomized controlled trial; women with singleton term pregnancies, cervical dilation ≥1 and subject satisfaction. 30 **Results:** One hundred and four received DVI (Group 1) alone and 104 DVI with

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ASM (Group 2). The rate of vaginal delivery within 24 h was 53% versus 56%, caesarean rate 8.7% versus 10.6% in Groups 1 and 2 respectively. Although the duration of labour was similar in both groups, about 6% of women required additional ripening with dinoprostone vaginal tablets in Group 2 compared to 11.5% in Group 1 (p-value = 0.2). The frequency of hyperstimulation syndrome, failed induction, analgesic requirements, and foetal outcomes were comparable.

Dr. Rupa Aherwar et al 2021, Background: This comparative study was conducted to compare the effectiveness of 25 µg of intravaginal misoprostol with intracervical cerviprime gel in terms of efficacy of drug, foeto-maternal outcome, side effects and complications of drugs. **Methods:** 100 primigravida at term; who were admitted for induction of labour were included in this study. They were randomly selected to receive either intravaginal misoprostol or intracervical cerviprime gel. 50 women received intravaginal 25 µg Misoprostol (Group A) every 6 hours for maximum of 5 doses and 50 women received 0.5 mg (2.5 ml) of intracervical cerviprime gel (Group B) till maximum of 3 doses. Comparison was done in terms of time taken for induction to delivery, mean time taken for onset of labour, APGAR score at 1 and 5 minutes and the neonatal outcome in either of the groups. **Results:** The mean time taken for onset of labour was less in the misoprostol group than in the cerviprime group (6.5 hours v/s 8 hours, P = 0.49). Similarly, duration from induction to delivery was less (20.08 ± 8.24 hours v/s 23.19 ± 9.59 hours, P >0.05) for misoprostol than cerviprime gel. Need for Oxytocin augmentation was less (16%) in misoprostol group as compared to cerviprime group (46%), P = 0.001. Caesarean section rate was slightly higher in misoprostol group (8% v/s 6%). Maternal complications were minimal in either group & the neonatal outcome was good in both the groups. The induction cost was much less in the misoprostol group. **Conclusions:** Compared to cerviprime gel; misoprostol is safe, efficacious, cheap, well tolerated drug by mother and foetus. It was found to be a better inducing agent, has short induction to delivery interval thus short duration of labour with similar maternal and foetal safety profile.

IV. AIM AND OBJECTIVES

The primary objective of the study is to determine whether the endocervical application of dinoprostone gel is safe and effective.

- To observe the therapeutic effect of Dinoprostone gel
- To observe and study the foeto-maternal outcomes
- To check the maternal health and neonatal health
- The secondary objective of the study is the analysis of pharmaco-economic expediency of administration of Dinoprostone gel
- To assess obstetrician's preference for induction of labour
- To study cost effectiveness of Dinoprostone gel

V. METHODOLOGY

The study was conducted in the Department of Obstetrics and Gynaecology, Government Cuddalore Medical College & Hospital (RMMCH), Annamalai University, Annamalai Nagar, Chidambaram-608002, Tamil Nadu. The study was conducted for a period of 6 months [November 2021 – April 2022].

The study was conducted for a period of 6 months (November 2021 – April 2022). The subjects were selected based on the inclusion and exclusion criteria. Informed consent form was obtained from patients prior to starting the study. The study was conducted among the patients who were admitted as inpatient under the department of OG, RMMCH. The dinoprostone gel details were collected. Neonatal health was checked using APGAR score. The net result of successful induction was recorded and tabulated. The report was analysed using suitable descriptive statistical tools. Report was submitted.

VI. OBSERVATION AND RESULTS

6.1 Primary Objectives

6.1.1 Data Based On Age Group

A total number of 180 patients were enrolled in the study. Among them the most common age group is 21-25 years (45%) followed by 26-30 years (35%) and others.

Table 1. Data Based On Age Group

Age group	No of patients	Percentage
15-20	21	11.70%
21-25	81	45%
26-30	63	35%
31-35	13	7.20%
36-40	2	1.10%
TOTAL	180	100.00%

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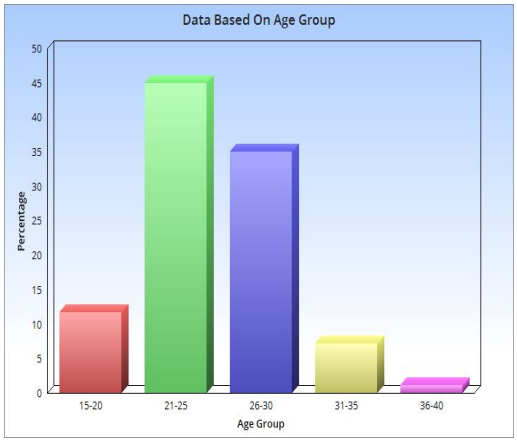

Figure 1: Data Based On Age Group

The demographic data shows that among these patients a high prevalence of pregnancy occurred in age group between 21 to 25 years at about 45%.

6.1.2 DATA BASED ON ABDOMINAL EXAMINATION

Table 2. Data based on Abdominal Examination

P/A	NO OF PATIENTS	PERCENTAGE
Head engaged	175	97.20%
Head unengaged	5	2.80%
TOTAL	180	100.00%
LOA position	178	98.90%
ROA position	2	1.10%
LOT position	0	0%
ROT position	0	0%
TOTAL	180	100.00%
Cephalic presentation	179	99.40%
Breech presentation	1	0.60%
Oblique presentation	0	0.00%
Transverse presentation	0	0.00%
TOTAL	180	100.00%

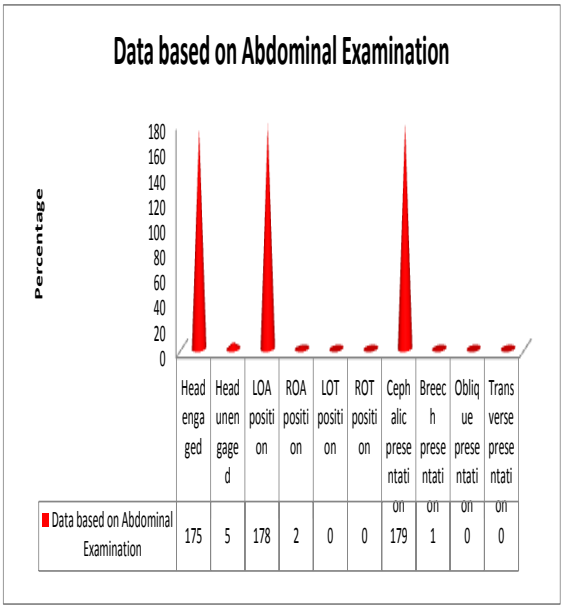

Figure.2 Data Based in Abdominal Examination

6.1.3 DATA BASED ON PELVIC EXAMINATION

Table 3:Pelvic Examination Details

P/V EXAMINATION	NO.OF	PERCEN
Membrane present	62	34.40%
Membrane not present	118	65.60%
TOTAL	180	100.00%
Inlet reached	13	7.20%
Inlet not reached	167	92.80%
TOTAL	180	100.00%
Pelvis gynaecoid	180	100.00%

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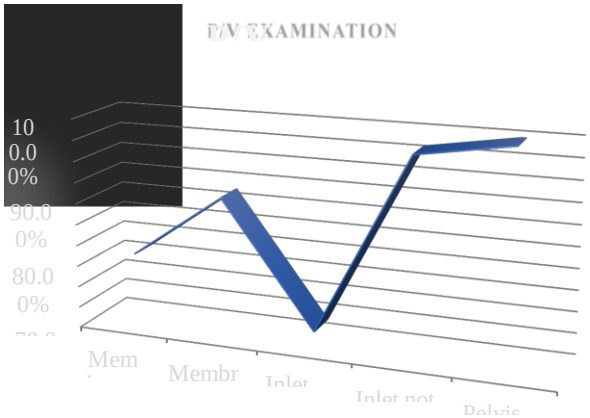

Figure 3:Graphical Representation On Pelvic Examination

From the above data we came to know that in majority of the patients the cervical membrane was not present and the pelvic inlet not reached which is about 65.60% and 92.80% respectively.

The abdominal examinations in labour are to determine the proposed examinations of the pelvic health. The results shows that most of the patients carried foetus with engaged head, positioned in LOA (Left Occiput Anterior) and with cephalic presentation.

6.1.4 DATA BASED ON CERVICAL EFFACEMENT

Table 4:Percentage of Cervical Effacement

EFFACEMENT	NO OF PATIENTS	PERCENTAGE
Cervix fully effaced	2	1.10%
Cervix 90% effaced	23	12.70%
Cervix 60% effaced	95	53%
Cervix 50% effaced	57	31.70%
Cervix not effaced	3	1.70%
TOTAL	180	100.00%

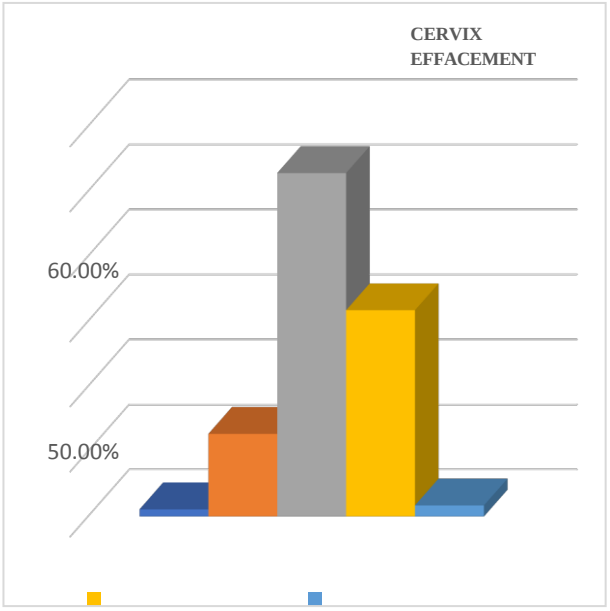

Figure 4: Bar Graph Representing Effacement Of Cervix

Among 180 patients, 53% of patient has 60% effaced cervix whereas 12.7% of patient has 90% effaced cervix.

6.1.5 DATA BASED ON DILATION OF CERVIX

Table 5: Percentage Of Cervical Dilation In Labour Patients

DILATION	NO OF PATIENTS	PERCENTAGE
Less than 6cm	106	58.90%
6cm-8cm	67	37.20%
8cm-10cm	7	3.90%
TOTAL	180	100.00%

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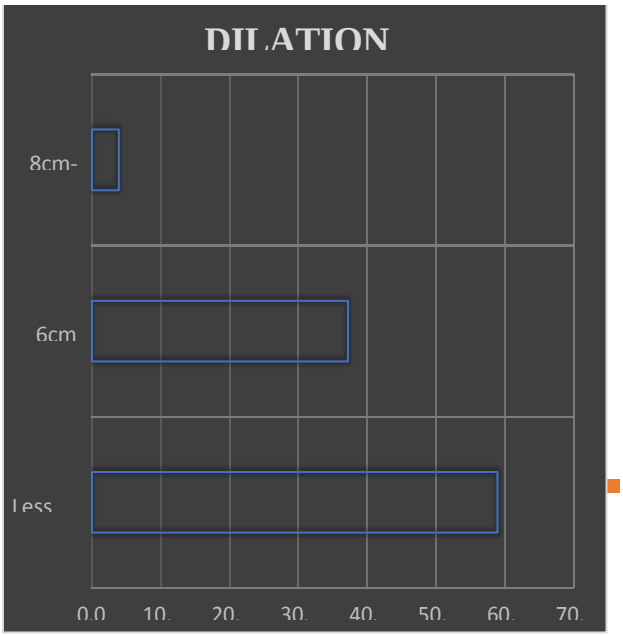


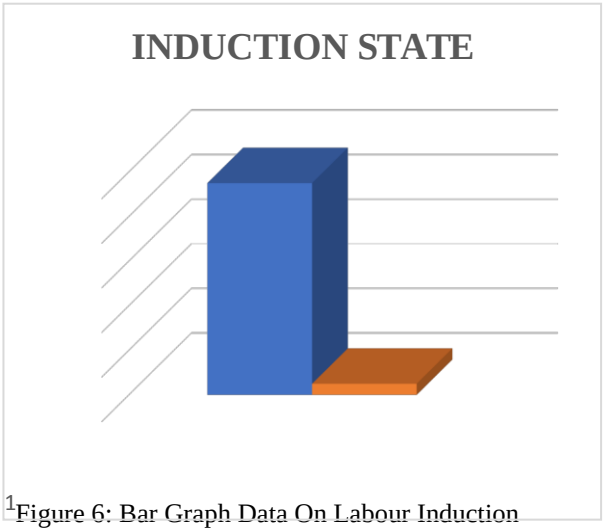
Figure 5: Graphical Representation Of Dilaton Of Cervix

Based on the above data more than 95% of patients were admitted with cervical dilation below 8cm (58.90% of patients with dilation below 6cm & 37.20% of patients with dilation between 6-8cm).

6.1.6 DATA ON INDUCTION STATE AFTER ENDOCERVICAL APPLICATION OF DINOPROSTONE GEL

Table 6: Data On Induction State After Endocervical Application Of Dinoprostone Gel

INDUCTION STATE	NO OF PATIENTS	PERCENTAGE
SUCCESS	171	95%
FAILURE	9	5.00%
TOTAL	180	100.00%



[1]Figure 6: Bar Graph Data On Labour Induction State

The data indicates that, involving the induction was performed by endocervical application of dinoprostone gel 171 patients (95%) effective and safe of mother and foetus among 180 patients.

6.1.7 DATA ON MOTHER & CHILD CONDITION

Table 7: Condition Of Mother & Child

Mother's Condition	No. of Labour Patients	%
Alive	180	100%
Dead	0	0
Child's Condition	No. of Child	%
Alive	180	100%
Dead	0	0%

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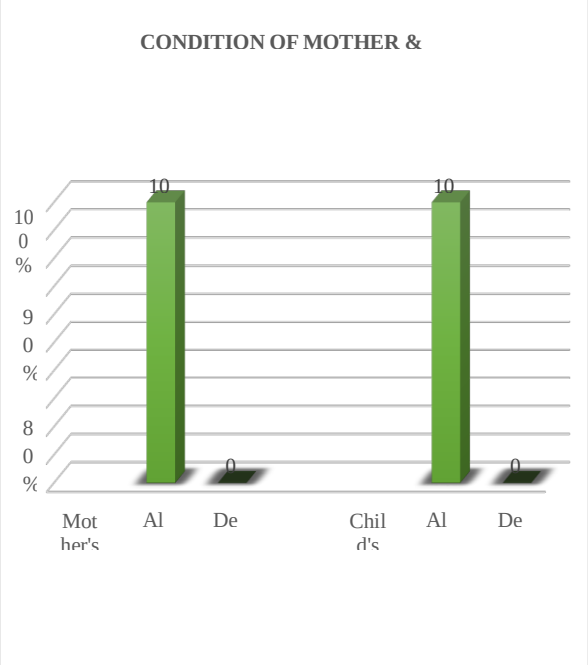

Figure 7: Bar Graph On Condition Of Mother & Child

Among 180 study subjects both the mother & the new born baby was alive (100%).

6.1.8 DATA BASED ON FETAL HEART RATE

Table 8. Data On Fetal Heart Rate

FHR	NO OF PATIENTS	PERCENTAGE
100-110	2	1.10%
110-120	0	0.00%
120-130	4	2.20%
130-140	21	11.70%
140-150	139	77.20%
150-160	13	7.20%
>160	1	0.60%
TOTAL	180	100.00%

About 77.20% of babies were born with 140-150/min heart rate among 180 newly born babies in the study after induction of labour.

6.2 Secondary Objectives

6.2.1 Cost Minimization Analysis

The drug we have used in the study is dinoprostone which is available in local pharmacies at various brands and the drugs we have taken for consideration for cost minimization analysis is Cerviprime & Dinost.

Table 9. Cost Minimization Analysis

BRANDS USED	COST	OUTCO	RESUL
CERVIPRIME (LOCAL PHARMACIES)	Rs.272	Same as others	×
DINOST (LOCAL PHARMACIES)	Rs.264	Same as others	×
CERVIPRIME (MAKKAL MARUNTHAGAM)	Rs.244	Same as others	✓

VII. CONCLUSION

Endocervical application of Dinoprostone gel is highly safe and successful in labour induction. The safety of Endocervical application of Dinoprostone gel was found to be 100%. Among 180 labour patients both mother & neonates were alive. The effectiveness of Endocervical application of Dinoprostone gel were found to be 95%. Among 180 labour patients 171 patients gave birth via Normal Vaginal Delivery. Only 5% failed induction had been observed and it led to LSCS. The observed Foetal Heart Rate & Apgar Score indicates the healthy neonates. Based on our Cost Minimization Analysis the least cost alternative drug is CERVIPRIME GEL which is sold at Makkal Marunthagam at Rs.244/-.

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