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**Dr. Nisiya KS**
Senior Resident, Department Of Obstetrics and gynecology, SUT Academy of Medical Sciences, Trivandrum, Kerala, India

**Dr. Uma Devi**
Professor and Head of the department, Department of Obstetrics and Gynecology, Santosh Hospital, Bangalore, Karnataka, India

**Dr. Farzana M Ahmed**
Senior consultant, Department of Obstetrics and Gynecology, Santosh Hospital, Bangalore, Karnataka, India

**Corresponding Author:**
**Dr. Nisiya KS**
Senior Resident, Department Of Obstetrics and gynecology, SUT Academy of Medical Sciences, Trivandrum, Kerala, India

# A prospective study on comparison of effectiveness and safety of dinoprostone intracervical gel and dinoprostone vaginal insert on induction of labour

**Dr. Nisiya KS, Dr. Uma Devi and Dr. Farzana M Ahmed**

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**Abstract**
**Background:** Labour induction is one of the most common obstetric procedures worldwide. There are a number of methods to induce labour, prostaglandins being the most effective one. The effects and properties of prostaglandins have been extensively investigated and many studies have compared the efficacy of different formulations available. There is a need to identify an effective method which is safe and cost effective associated with ease of introduction and removal in the event of complications. A method which reduces the number of vaginal examination thereby decreasing patient discomfort and doctor's workload should be considered. Hence the purpose of this study is to compare the efficacy, safety and acceptability (doctor and patient) of dinoprostone intracervical gel and dinoprostone vaginal insert.
**Materials and Methods:** In this prospective comparative study, 120 pregnant women undergoing procedure of induction of labour in Santosh Hospital from September 2017 to May 2019 were assigned randomly to two groups, dinoprostone intracervical gel and dinoprostone sustained release intravaginal insert. Group A received 500 mcg of dinoprostone gel intracervically at 6th hourly intervals till active labour ensue for a maximum of 3 doses. Group B received ten milligrams of dinoprostone vaginal insert for single application for maximum of 24 hours.
**Results:** Induction delivery interval was significantly lower (p value-<0.001) in dinoprostone vaginal insert group than with intracervical gel group. Need for oxytocin was lesser (p value-<0.001) when dinoprostone vaginal insert was used compared to intracervical gel. No significant difference between two groups was found on caesarean section rate (p value-0.803). Rate of hyperstimulation was high in dinoprostone vaginal insert group, while there was no significant difference noted in meconium stained liquor (p value-0.729) and postpartum hemorrhage (p value-0.648) between 2 groups. The patient acceptability was found to be higher in dinoprostone vaginal insert group as there was less intensity of labour pain (p value-<0.001) in 1st stage of labour and decreased number of pervaginal examinations. Fetal outcome in each case was assessed with APGAR score at 1 and 5 minutes after the delivery of the fetus and no significant difference were found in both the groups.
**Conclusion:** Dinoprostone intracervical gel and dinoprostone vaginal insert are safe and efficacious methods of induction of labour. However intravaginal insert was found to be easy to use and more efficacious method of induction with less pain during the initial hours of active labour. The method of induction should be individualized based on affordability and patient acceptability**.**

**Keywords:** Induction of labour, prostaglandins, dinoprostone pessary/vaginal insert, dinoprostone gel, PGE2

## Introduction
Labour induction is one of the most common obstetric procedures worldwide [1]. The incidence of labour induction for reducing the duration of pregnancy has continued to rise since several decades. In developed countries, the proportion of infants delivered at term following induction of labour can be as high as one in four deliveries [2]. Unpublished data from the WHO Global Survey on Maternal and Perinatal Health, which included 373 health-care facilities in 24 countries and nearly 300 000 deliveries, showed that 9.6% of the deliveries involved labour induction. Overall, the survey found that facilities in African countries tended to have lower rates of induction of labour (lowest: Niger, 1.4%) compared with Asian and Latin American countries (highest: Sri Lanka, 35.5%) [2].
There are a number of methods to induce labour surgically, mechanically or pharmacologically, PGE being the most effective one [3]. The effects and properties of PGE2 have been extensively investigated and many studies have compared the efficacy of different formulations available

[4]. Dinoprostone gel (0.5 mg) has been successfully used by obstetricians all over the world [5]. A consistent controlled release of 0.3mg/hour of dinoprostone can be achieved through the use of vaginal inserts with least incidence of hyperstimulation [5]. Use of dinoprostone vaginal insert in the Indian scenario would be a beneficial study.

A study reported that slow-release PGE2 vaginal insert achieved cervical ripening and subsequent delivery over a shorter time period [6]. Conversely, another study declared PGE2 vaginal gel was superior for the induction of labor [7]. As mentioned above, when it comes to which formulation is optimal, there is an extremely fierce ongoing debate on the preparations of PGE2 [5]. There is a need to identify an effective method which is safe and cost effective associated with ease of introduction and removal in the event of complications. A method which reduces the number of vaginal examination thereby decreasing patient discomfort and doctor's workload should be considered. Hence the purpose of this study is to compare the efficacy, safety and acceptability (doctor and patient) of dinoprostone intracervical gel and dinoprostone vaginal insert.

## Materials and methods

This prospective comparative study was carried out on patients of Department of Obstetrics and Gynecology at Santosh Hospital, Bangalore, India from September 2017 to May 2019. 120 pregnant women undergoing procedure of induction of labour with dinoprostone intracervical gel and dinoprostone vaginal insert in Santosh hospital

**Study Design:** Prospective comparative study.

**Sample size:** 120 patients.

**Sample size calculation:** Taking 8% as global prevalence for induction of labour and 5% as the level of significance with 95% confidence interval, the required sample size was 114.

$n=Z^2_{1-\alpha/2}\ P\ (1-P)\ /\ d^2$

$Z^2_{1-\alpha/2}$ is standard normal value, 5% level of significance =1.96

P is prevalence that is 8% which equals to 0.08

d is absolute precision which is 5% which equals to 0.05

So, n becomes 114

Total number of patients included in the study-120 rounding off) 120subjects (Two groups of 60 patients each – one group induced with dinoprostone intracervical gel and dinoprostone vaginal insert).

**Sample Design**: Random number sampling

**Inclusion criteria:**

1. Singleton pregnancy
2. >37 weeks GA
3. Cephalic
4. Bishop's score less than 4
5. Matched samples of primigravidae and mulitigravidae
6. Medical Indications of induction (matched samples of parity and gestational age)
7. Willing to give informed written consent to be a part of the study.

**Exclusion criteria**

1. Patient with preexisting spontaneous labour.
2. Previous uterine scar
3. Vaginal bleeding
4. Fetal heart rate abnormalities
5. A medical condition that would preclude dinoprostone administration

**Methodologies and Type of Data Collection**

Following Ethical Committee approval and clearance, all cases undergoing labour induction with dinoprostone gel and vaginal insert were assessed for onset of labour, improvement in Bishop' sscore, time till vaginal delivery, caesarean section rate, Postpartum Hemorrhage, uterine hyperstimulation /hypertonus /tachysystole, fetal heart rate variations.

**Procedure**

Patients who fulfilled the criteria for study were counseled about the risks and benefits of induction of labour and the induction agents.From patients who were willing to take part in the study, written informed consent was obtained from the patients and their close relatives.Women were randomly allocated in two groups to receive dinoprostone as either a vaginal gel (Group A) or as a vaginal insert (Group B). Induction was started after taking a CTG of the patient. Group A received 0.5 mg of endocervical dinoprostone gel under all aseptic precautions which was repeated after 6 hours when active labour did not ensue. In Group B 10-mg controlled-release dinoprostone pessary was placed in the posterior fornix of the vagina in a transverse position under all aseptic precautions.In both the above groups Improvement in bishop's score was assessed.

The pessary was removed under following conditions

- after 24 hours
- if active labor ensued
- when membrane ruptured
- non reassuring fetal heart rate
- hyperstimulation/ Hypertonicity/ tachysystole were present.

In all cases, fetal heart rate and uterine activity was recorded for 1 hour after the application of dinoprostone, and thereafter every hourly fetal heart rate assessed for minimum of 1 minute. After 4 hours of induction CTG trace for 20 minutes were taken to check reassuring fetal heart rate along with contraction if any. Active labor was considered to be established when there was at least three to four regular uterine contractions during a 10-minute period each lasted for 30-45 seconds, and the cervix was well effaced and >/= 3 cm dilated. Incidence of hyperstimulation/Hypertonicity/ tachysystole was noted if any. All women not in active labor was re-assessed after 6 hours of dinoprostone insertion and bishops score was noted. Total number of doses of intracervical gel is documented. For augmentation of labour oxytocin was started 6 hours from the last insertion of intracervical gel and 30 minutes after the removal of intravaginal insert. During the initial hours of active labour, pain was assessed with visual analogue scoring system which has grades till 10.Progress of labour was plotted in partogram and those who were crossing the action line was taken for caesarean section. Duration of each stage of labour was noted. Use of extra drugs like labour analgesics which are also acting as cervical dilators and cervical dilators like valethe mate bromide and drotaverine hydrochloride in both the groups were documented. The mode of delivery was noted. Incidence of postpartum hemorrhage, meconium stained liquor and caesarean section rate was noted. Neonatal APGAR score at 5 minutes and 10 minutes were documented. Baby's birth weight and requirement of admission to NICU was documented Patient was asked about the satisfaction score whether the induction method was good or bad on the day of discharge and the reasons were documented.

**Statistical analysis**

The following methods of statistical analysis have been used in this study. The data collected was entered in Microsoft Excel and Statistical analyses were performed using the Statistical Package for Social Science (SPSS version 18.5) software. The results for each parameter (numbers and percentages) for discrete data and averaged (mean ± standard deviation) for each parameter were presented in tables and figures. Proportions were compared using Chi-square test of significance. The student't' test was used to determine whether there was a statistical difference between dinoprostone intracervical gel and intravaginal insert groups in the parameters measured. In all above test p value less than 0.05 was taken to be statistically significant

**Results**

A total of 120 patients were allocated in the study with group A being the patients who were induced with intracervical gel and group B, being induced with intravaginal insert. Both the samples were ideally matched as shown in the table 1. Out of 120 patients induced 27 patients were having bishop's score of 1, 50 patients were having bishop's score of 2 and 43 patients were having bishop's score of 3 as shown in table 2 and 3.

**Table 1:** characteristics of ideally matched samples

| characteristics | Group A (intracervical gel) | group B (intravaginal insert) | p value |
|---|---|---|---|
| **Mean age** | 25.6+/-3.724 | 26.1+/-3.976 | 0.508 |
| Mean Gestational age | 39.3+/-0.751 | 39.5+/-0.724 | 0.140 |
| Mean BMI | 26.6+/-2.225 | 26.9+/-2.131 | 0.521 |
| Number of primigravida | 36 | 36 | 1.0 |
| Number of multigravida | 24 | 24 | 1.0 |

**Table 2:** Distribution of Bishop's score between the study groups in Primigravidae

| | Bishops Score | | | Total | $\chi^2$ value | P value |
|---|---|---|---|---|---|---|
| | 1 | 2 | 3 | | | |
| Group A | 14 | 17 | 5 | 36 | 2.754 | 0.252 |
| | 38.9% | 47.2% | 13.9% | 100.0% | | |
| Group B | 9 | 17 | 10 | 36 | | |
| | 25.0% | 47.2% | 27.8% | 100.0% | | |
| Total | 23 | 34 | 15 | 72 | | |
| | 31.9% | 47.2% | 20.8% | 100.0% | | |

**Table 3:** Distribution of Bishop's Score between the study groups in Multigravidae

| | Bishops Score | | | Total | $\chi^2$ value | P value |
|---|---|---|---|---|---|---|
| | 1 | 2 | 3 | | | |
| Group A | 2 | 9 | 13 | 24 | 0.393 | 0.822 |
| | 8.3% | 37.5% | 54.2% | 100.0% | | |
| Group B | 2 | 7 | 15 | 24 | | |
| | 8.3% | 29.2% | 62.5% | 100.0% | | |
| Total | 4 | 16 | 28 | 48 | | |
| | 8.3% | 33.3% | 58.3% | 100.0% | | |

**Table 4:** Comparison of mode of delivery between two groups

| | Mode of Delivery | | Total | $\chi^2$ value | P value |
|---|---|---|---|---|---|
| | Vaginal | LSCS | | | |
| Group A | 50 | 10 | 60 | 0.063 | 0.803 |
| | 83.3% | 16.7% | 100.0% | | |
| Group B | 51 | 9 | 60 | | |
| | 85.0% | 15.0% | 100.0% | | |
| Total | 101 | 19 | 120 | | |
| | 84.2% | 15.8% | 100.0% | | |

**Table 5:** Comparison of duration for improvement in Bishop's Score >/=6 between primigravida and multigravida in both the groups

| Obstetric score | Group | N | Mean | SD | Median | Min. | Max. | 't' value | 'p' value |
|---|---|---|---|---|---|---|---|---|---|
| Primigravida | Group A | 27 | 543.0 | 299.163 | 480 | 180 | 1400 | 9.554 | ***0.003*** |
| | Group B | 28 | 364.3 | 63.095 | 360 | 240 | 540 | | |
| Multigravida | Group A | 23 | 451.3 | 228.738 | 360 | 180 | 900 | 8.859 | ***0.005*** |
| | Group B | 23 | 289.6 | 124.881 | 240 | 180 | 720 | | |

**Table 6:** Comparison of time of insertion of the agent to onset of active labour (minutes) between 2 groups among primigravida and multigravida

| Obstetric score | Group | N | Mean | SD | Median | Min. | Max. | 't' value | 'p' value |
|---|---|---|---|---|---|---|---|---|---|
| Primigravida | Group A | 27 | 777.8 | 335.506 | 780 | 180 | 1320 | 31.288 | ***<0.001*** |
| | Group B | 28 | 379.3 | 168.960 | 360 | 180 | 960 | | |
| Multigravida | Group A | 23 | 584.3 | 245.539 | 600 | 180 | 960 | 16.517 | ***<0.001*** |
| | Group B | 23 | 328.7 | 175.274 | 240 | 180 | 900 | | |

**Table 7:** Comparison of duration of active phase (minutes) between 2 groups

| Obstetric score | Group | N | Mean | SD | Median | Min. | Max. | 't' value | 'p' value |
|---|---|---|---|---|---|---|---|---|---|
| Primigravida | Group A | 27 | 319.1 | 115.592 | 320.0 | 120 | 530 | 177.160 | *<0.001* |
| | Group B | 28 | 27.4 | 9.363 | 26.5 | 13 | 46 | | |
| Multigravida | Group A | 23 | 162.1 | 100.050 | 120.0 | 56 | 430 | 49.504 | *<0.001* |
| | Group B | 23 | 15.1 | 5.455 | 15.0 | 7 | 30 | | |

In both primigravidae and multigravida patients active phase was significantly shorter with dinoprostone intravaginal insert when compared with intracervical gel.

**Table 8:** Comparison of time of insertion to vaginal delivery (minutes) between 2 groups

| Obstetric score | Group | N | Mean | SD | Median | Min. | Max. | 't' value | 'p' value |
|---|---|---|---|---|---|---|---|---|---|
| Primigravida | Group A | 27 | 1349.0 | 520.553 | 1408 | 365 | 2183 | 19.942 | ***<0.001*** |
| | Group B | 28 | 845.3 | 286.989 | 766 | 423 | 1380 | | |
| Multigravida | Group A | 23 | 1142.6 | 539.134 | 1042 | 512 | 2900 | 11.925 | ***<0.001*** |
| | Group B | 23 | 684.1 | 338.663 | 510 | 240 | 1480 | | |

**Table 9:** Comparison of requirement of oxytocin between 2 groups during labour

| | Requirement of Oxytocin | | Total | $\chi^2$ value | P value |
|---|---|---|---|---|---|
| | Yes | No | | | |
| Group A | 40 | 9 | 49 | 40.942 | ***<0.001*** |
| | 81.6% | 18.4% | 100.0% | | |
| Group B | 9 | 42 | 51 | | |
| | 17.6% | 82.4% | 100.0% | | |
| Total | 49 | 51 | 100 | | |
| | 49.0% | 51.0% | 100.0% | | |

**Table 10:** Distribution of incidence of hyperstimulation between the study groups in primigravida

| | Hyperstimulation | | Total | $\chi^2$ value | P value |
|---|---|---|---|---|---|
| | Present | Absent | | | |
| Group A | 1 | 27 | 28 | 0.352 | 0.553 |
| | 3.6% | 96.4% | 100.0% | | |
| Group B | 2 | 26 | 28 | | |
| | 7.1% | 92.9% | 100.0% | | |
| Total | 3 | 53 | 56 | | |
| | 5.4% | 94.6% | 100.0% | | |

**Table 11:** Distribution of hyperstimulation between the study groups in Multigravida

| | Hyperstimulation | | Total | $\chi^2$ value | P value |
|---|---|---|---|---|---|
| | Present | Absent | | | |
| Group A | 1 | 22 | 23 | 1.095 | 0.295 |
| | 4.3% | 95.7% | 100.0% | | |
| Group B | 3 | 20 | 23 | | |
| | 13.0% | 87.0% | 100.0% | | |
| Total | 4 | 42 | 46 | | |
| | 8.7% | 91.3% | 100.0% | | |

Though incidence of hyperstimulation did not show any significant difference between two groups, hyperstimulation was seen more with intravaginal insert when compared with intracervical gel group (5 vs. 2). Incidence of hyperstimulation was seen more in multigravida than in primigravida.

**Table 12:** Comparison of onset of hyperstimulation after insertion of the agent in minutes

| Group | N | Mean | SD | Median | Min. | Max. | 't' value | 'p' value |
|---|---|---|---|---|---|---|---|---|
| Group A | 2 | 322.5 | 31.820 | 323 | 300 | 345 | 0.070 | 0.801 |
| Group B | 5 | 372.0 | 248.837 | 300 | 180 | 780 | | |

Even though the onset of hyperstimulation after the insertion of drugs did not show much difference, hyperstimulation was set in, in a shorter period with intracervical gel when compared with intravaginal insert. But the incidence of hyperstimulation was high in intravaginal insert group.

**Table 13:** Comparison of indication for LSCS after the insertion of the agent between 2 groups

| | Indication for LSCS | | | | Total | $\chi^2$ value | P value |
|---|---|---|---|---|---|---|---|
| | CPD | MSL | NPL | NRFHR | | | |
| Group A | 0 | 2 | 7 | 1 | 10 | 7.947 | 0.094 |
| | 0% | 20.0% | 70.0% | 10% | 100.0% | | |
| Group B | 3 | 3 | 2 | 1 | 9 | | |
| | 33.3% | 33.3% | 22.2% | 11.1% | 100.0% | | |
| Total | 3 | 5 | 9 | 2 | 19 | | |
| | 15.8% | 26.3% | 47.4% | 10.5% | 100.0% | | |

Non progression of labour / failed induction was seen more with intracervical gel.

**Table 14:** Comparison of incidence of PPH after insertion of the agent between 2 groups

| | PPH | | Total | $\chi^2$ value | P value |
|---|---|---|---|---|---|
| | Present | Absent | | | |
| Group A | 3 | 57 | 60 | 0.209 | 0.648 |
| | 5.0% | 95.0% | 100.0% | | |
| Group B | 2 | 58 | 60 | | |
| | 3.3% | 96.7% | 100.0% | | |
| Total | 5 | 115 | 120 | | |
| | 4.2% | 95.8% | 100.0% | | |

The incidence of postpartum hemorrhage did not show any significant difference between the two groups.

**Table 15:** Comparison of incidence of meconium stained liquor after the induction between 2 groups

| | Meconium Stained Liquor | | Total | $\chi^2$ value | P value |
|---|---|---|---|---|---|
| | Present | Absent | | | |
| Group A | 4 | 56 | 60 | 0.120 | 0.729 |
| | 6.7% | 93.3% | 100.0% | | |
| Group B | 5 | 55 | 60 | | |
| | 8.3% | 91.7% | 100.0% | | |
| Total | 9 | 111 | 120 | | |
| | 7.5% | 92.5% | 100.0% | | |

There was no statistically significant difference between the two groups in the incidence of hyperstimulation.

**Table 16:** Comparison of use of extra drugs for dilatation of cervix during active phase of labour between 2 groups

| | Extra Drug Given | | Total | $\chi^2$ value | P value |
|---|---|---|---|---|---|
| | Yes | No | | | |
| Group A | 46 | 4 | 50 | 48.414 | **<0.001** |
| | 92.0% | 8.0% | 100.0% | | |
| Group B | 12 | 39 | 51 | | |
| | 23.5% | 76.5% | 100.0% | | |
| Total | 58 | 43 | 101 | | |
| | 57.4% | 42.6% | 100.0% | | |

92 percent patients among intracervical gel group required extra drugs like labour analgesics and cervical dilators in active phase of labour. But only 23.5% patients in intravaginal insert group required those drugs in active phase of labour.

**Table 17:** Comparison of APGAR score of neonates at 5 minutes and 10 minutes between 2 groups

| | Group | N | Mean | SD | Median | Min. | Max. | 't' value | 'p' value |
|---|---|---|---|---|---|---|---|---|---|
| APGAR Score at 5 min | Group A | 60 | 7.5 | 0.792 | 8 | 5 | 8 | 1.476 | 0.227 |
| | Group B | 60 | 7.4 | 0.709 | 7 | 5 | 8 | | |
| APGAR Score 10 min | Group A | 60 | 9.5 | 0.748 | 10 | 7 | 10 | 0.763 | 0.384 |
| | Group B | 60 | 9.4 | 0.715 | 10 | 7 | 10 | | |

There was no significant difference between the two groups in APGAR score of babies at 5 minutes and 10 minutes

**Table 18:** Comparison of birth weight between 2 groups

| Group | N | Mean | SD | Median | Min. | Max. | 't' value | 'p' value |
|---|---|---|---|---|---|---|---|---|
| Group A | 60 | 3,096.5 | 371.382 | 3,020 | 2450 | 3890 | 0.277 | 0.599 |
| Group B | 60 | 3,133.4 | 392.431 | 3,100 | 2400 | 3900 | | |

**Table 19:** Comparison of NICU admission between two groups

| | NICU Admission | | Total | $\chi^2$ value | P value |
|---|---|---|---|---|---|
| | Yes | No | | | |
| Group A | 4 | 56 | 60 | 0.152 | 0.697 |
| | 6.7% | 93.3% | 100.0% | | |
| Group B | 3 | 57 | 60 | | |
| | 5.0% | 95.0% | 100.0% | | |
| Total | 7 | 113 | 120 | | |
| | 5.8% | 94.2% | 100.0% | | |

There was no significant difference between the two groups in need for NICU admission in newborns

**Table 20:** Comparison of patient satisfaction between 2 groups

| | Satisfaction Score | | Total | $\chi^2$ value | P value |
|---|---|---|---|---|---|
| | Good | Bad | | | |
| Group A | 47 | 13 | 60 | 0.484 | 0.487 |
| | 78.3% | 21.7% | 100.0% | | |
| Group B | 50 | 10 | 60 | | |
| | 83.3% | 16.7% | 100.0% | | |
| Total | 97 | 23 | 120 | | |
| | 80.8% | 19.2% | 100.0% | | |

78.3% Patients in intracervical gel group and 83.3% patients in intravaginal insert group were satisfied with the induction methods.

**Table 21:** Comparison of VAS for pain during initial 6 hours of labour

| | VAS initial 6 hours of active labour | | Total | $\chi^2$ value | P value |
|---|---|---|---|---|---|
| | <-5 | >5 | | | |
| Group A | 15 | 45 | 60 | 17.877 | *<0.001* |
| | 25.0% | 75.0% | 100.0% | | |
| Group B | 38 | 22 | 60 | | |
| | 63.3% | 36.7% | 100.0% | | |
| Total | 53 | 67 | 120 | | |
| | 44.2% | 55.8% | 100.0% | | |

75 percentage of intracervical gel group patients had more pain with VAS> 5 in initial 6 hours of active labour where as 25% patients had VAS <5 during initial 6 hours of active labour. There was significant difference in this parameter in case of intravaginal insert. Majority of the patients (63.3% patients) had VAS <5 whereas 36.7% of intravaginal insert group had VAS>5

## Discussion

The aim of the study was to evaluate and compare the efficacy, safety and patient satisfaction between 2 formulations of the same drug dinoprostone on induction of labour. The study was done on 120 patients in which 60 were belonging to dinoprostone vaginal pessary group and the rest 60 were belonging to dinoprostone gel group. All patients were booked case of Santosh Hospital who were having regular antenatal checkup.

Local application of dinoprostone is commonly used for cervical ripening. It is available in 3 different forms worldwide, a gel sustained release pessary and vaginal tablets. In India only 2dinoprostone intracervical gel was available. A 10mg sustained release dinoprostone vaginal insert or pessary was introduced and was licensed in India since June 2016 (government of India, central drug standardized control, registration number RC/FF-002002) [8]. Various studies were done comparing all the different formulations of dinoprostone for induction of labour with each other as well as different methods.

Selected cases were primigravidae and multigravidae who were matching in age, gestational age and BMI to avoid any bias. Hence there was no statistical difference between two groups in age, gestational period at the time of induction and body mass index of women considering the pre pregnancy weight.

In each group,36 primigravidae were selected who were matching in age and BMI with the other group and 24 multigravidae who were matching in age, parity and BMI with

the other group.

Indications for induction of labour were similar in both the groups. Among 60 cases who were induced with dinoprostone intracervical gel, 8 patients were induced in view of hyperglycemia in pregnancy, 7 patients were induced in view of hypertensive disorder in pregnancy, 4 were induced for Oligoamnios and 41 patients for pregnancies who neared their expected date of delivery. A total of 60 patients were induced with dinoprostone vaginal insert. Maximum numbers of cases [9] were induced for pregnancies that neared the expected date of delivery but did not have any risk factors or comorbidities. 7 pregnant ladies were induced with dinoprostone insert in view of hyperglycemia in pregnancy and 8 were induced in view of hypertensive disorder in pregnancy and 4 were induced for Oligoamnios.In study done by Swati Garg *et al.* postdated pregnancy was the major indication in both the groups and the rest were preeclampsia GDM, IUGR and others like Oligohydramnios, Rh iso-immunisation, PROM and maternal request [8].

The success of induction is strictly dependent on the cervical status either assessed by Bishop score or by sonographic measurement of cervical length [10]. Various studies compared these two methods of cervical assessment but failed to show advantage of any of the two compared to the other in the prediction of vaginal delivery. In this study we used Bishop's score of less than 4as one of the inclusion criteria for the selection of patient.16 patients were having bishop's score of 1, 26 patients with score of 2 and 18 patients with score of 18 in the intracervical gel group.11 patients, 24 patients and 25 patients of bishop's score 1,2 and 3 respectively included in the intravaginal insert group.

The maximum number of dose for intracervical gel is 3 according to American College of Obstetricians and Gynecologists. Maya Menon *et al.* proved in their study that the maternal and fetal outcomes were better with one or two doses of PGE2 gel. Third dose of PGE2 gel unnecessarily prolonged the duration of labour leading to increased emergency caesarean section and increased neonatal intensive care unit admissions (NICU) [11]. In our study we used only 1 dose for 26 patients, 2 doses for 31 patients and 3 doses for 3 patients out of 60 patients in total. Dinoprostone vaginal insert is single dose 24 hour sustained release which can be kept for maximum of 24 hours.In our study 50 patients in intracervical gel group and 51 patients in intravaginal insert group delivered vaginally.

One of the criteria for determining the effectiveness of the drug was the rate of successful vaginal delivery after induction. 83.3% patients delivered vaginally among intracervical gel group and 85% patients delivered vaginally in intravaginal insert group. Hence when compared there was no statistical difference in the mode of delivery with a p value of 0.803 and chi square value 0.063. But the rate of caesarean section was more with the use of intracervical gel (37%) as compared to vaginal pessary (29%) in the study done by Swati Garg *et al.* in 2018 (8).

The duration of Bishop's score improvement to more than or equal to 6 from the insertion of the induction agent irrespective of the initial score at the time of insertion was the second criteria to compare the effectiveness. This parameter indirectly shows the duration for cervical priming. Kalkat *et al.* found that the Bishop's score change of >3 in 24 h (Propess 83.3% vs. Prostin 73.3%, p value=0.19) did not show statistically significant difference in the two groups [12]. In our study, the improvement was shown faster with dinoprostone vaginal insert than dinoprostone intracervical gel with a p value of <0.001. There was a statistical difference in primigravidae with mean duration for improvement in bishops score of 364.3 minutes with intravaginal insert when compared with intracervical gel which took 543 minutes for the same (p value- 0.003). In multigravidae also the trend remained same with a p-value of<0.005. The mean duration of improvement of Bishop's score with intracervical gel was 451.3minutes which was longer when compared with intravaginal insert where improvement was shown in 289.6 minutes.

The time of onset of active labour with 3 strong contractions in 10 minutes each lasting for 30 – 45 seconds after induction was the third criteria for comparison of effectiveness for the agents. Intracervical gel took an average of 688.8 minutes for the onset of active labour whereas intravaginal insert took 356.5 minutes. This was statistically significant with p value of <0.001.When primigravidae patients were alone compared between 2 groups for the same parameter, the minimum time for onset of labour after insertion of intracervical gel was 180 minutes and maximum time was 1320 minutes which gave a mean of 777.8 minutes. This was statistically longer than that with intravaginal insert even though the minimum time for onset of labour was the same (180 minutes) and the maximum time was 960 minutes with a mean duration of 379.3 minutes. The p value was <0.001. the same parameter when compared among multigravidae showed the same trend with shorter duration for intravaginal gel when compared with intracervical gel with mean value 328.7 vs 584.3 with p value <0.001. However the conclusion reached by Sanchez-Ramos *et al.* was opposite, wherethey found the dinoprostone vaginal insert less effective than other prostaglandin preparations in the induction of active labour [13]

One striking secondaryoutcome wasthe duration of active phase was significantly lesser when intravaginal insert was used with a p value of <0.001. The maximum duration of active phase of 2nd stage of labour was 46 minutes and the minimum duration was 7 minutes whereas when intracervical gel was used the average duration of active phase was 246.9 with a minimum duration of 50 minutes and maximum duration up to 530 minutes. When primigravidae were compared the mean duration was more than multigravidae for both the groups. The primigravidae showed a mean active phase of 319.1minutes and 21.1 minutes with intracervical gel and intravaginal insert respectively. This was statistically highly significant with p value of <0.001. In multigravidae, the intravaginal insert reduced the active phase significantly with mean duration of 15.1 minutes when compared with intracervical gel with mean value of 162.1 minutes. The p value for multigravidae was <0.001.

Various studies were done to find out the difference in induction delivery interval until now. The results were varying. Study done by Xian ling *et al.* showed that dinoprostone vaginal insert has distinct superiority in terms of VD within 24 h (OR = 2.35, 95% CI = 1.34, 4.13, p=0.003 ) and had an advantage of a shorter hospital stay (41% and 46% ) and less postpartum hemorrhage in contrast to gel (13%,23%) (6). But the mean time interval from induction to vaginal delivery did not differ between the similar groups in the comparative study done by D'Aniello *et al.* despite being shorter for the pessary group in induction–delivery intervals > 12 h (14). In our study induction delivery interval was significantly reduced with intravaginal insert with mean duration of 772.6 minutes when compared with intracervical gel with mean duration of 1254 minutes and the p value was <0.001 in our study. Among primigravidae patients, the mean induction delivery interval was significantly reduced (845.3 minutes) with intravaginal insert when compared with intracervical gel1349 minutes with p value of <0.001. When the induction delivery interval was compared among multigravidae

patients, the trend was not different. The mean interval was significantly shorter with intravaginal insert (684.1 minutes) when compared with intracervical gel (1142.6minutes) with a pvalue of <0.001.

Facchinetti *et al.* in 2005 found that more women in the cervical gel group (41.4%, as against 24.3% in the vaginal insert group; Chisquare 3.92, P = 0.48) needed oxytocin for labour induction, giving an OR of 2.21 (95% CI = 1.07–4.55) [15]. The result in our study was not different. There was statistically significant difference between 2 groups in the use of oxytocin for augmentation of labour with a p value of <0.001. Among 49 patients who delivered vaginally with intracervical gel, 40 patients (81.6%) required oxytocin whereas among 51 patients who delivered vaginally with intravaginal insert only 9 patients required oxytocin (17.6%).

The safety of induction agents were studied in terms of number of parameters. Incidence of hyperstimulation was one of the parameters. Hyperstimulation can be diagnosed when tachysystole or Hypertonicity is present. Tachysystole was defined as more than or equal to 5 contractions in 10 minutes each lasting for 30 – 45 seconds. Hypertonicity was defined as each contraction lasting for more than 1 minute. Even though the incidence of hyperstimulation was statistically insignificant, it was seen higher with intravaginal insert than with intracervical gel (5 versus 2). The onset of hyperstimulation after the insertion for both the agents was similar with a mean of 322.5 minutes and 372 minutes for intracervical gel and intravaginal insert respectively. In most of the studies this result was similar.

Safety of induction agents were studied in terms of the caesarean section rate too. There was no significant difference in the rate of caesarean section between two groups with p value of 0.803. Out of 60 patients induced with intracervical gel 10 patients (16.7%) could not successfully deliver vaginally and they were taken for lower segment caesarean section. The most common indication for LSCS was non progression of labour or failed induction which was seen in 7 patients out of 10 in intracervical gel group.The other indications were meconium stained liquor which was seen in 2 patients and non-reassuring fetal heart rate seen in 1 patient. Among 60 patients induced with intravaginal insert, 9 patients delivered with lower segment caesarean section (15%). 3 patients underwent caesarean section as they were diagnosed as having cephalopelvic disproportion when assessed during labour. 3 patients had meconium staining of liquor, 2 had failed induction and 1patient went for LSCS due to non-reassuring fetal heart rate. The 2 groups did not show much difference on indications of caesarean section with a p value of 0.094.

One of the criteria for determining safety of induction agents was the incidence of postpartum hemorrhage. Out of 120 patients who underwent induction 5 (4.2%) patients had PPH. Among them 3 patients were induced with intracervical gel and 2 patients were induced with intravaginal insert. Hence there was no statistical difference between 2 induction agents in this criteria with a p value of 0.648.

Incidence of meconium stained liquor was 7.5 percent (9 patients) in the study. Out of that 4 patients were from intracervical gel group and the rest 5 patients were from intravaginal insert group. This was statistically insignificant with a p value of 0.729.

In labour rooms it is commonly seen the use of some extra drugs for dilation of cervix which will also help in pain relief. Various drugs have been tried to increase the cervical dilatation, so that hazards of prolonged labour for both mother and fetus are minimized without increasing maternal or perinatal mortality and morbidity [16]. Valethemate bromide has neurotropic and musculotropic actions, resulting in relaxation of cervical musculature leading to quick dilatation of cervix and shortened labour [17]. Drotaverine hydrochloride also shortens the duration of labour. Anafortan (camylofin hydrochloride) is a selective PDE-4 enzyme inhibitor which facilitates cervical effacement and dilatation, accelerates labour, regulated the ANS and thereby prevents disordered progress of labour. Tramadol hydrochloride is a good labour analgesic as well as a cervical dilator [18]. Buscopan (hyoscine-butyl- N- bromide) and scopolamine have been used for pain relief and shortening of labour [19]. Some of these drugs are commonly used in Santosh Hospital labour room. There was statistically significant difference in the use of these extra drugs with a p value of <0.001. Only 12 patients (23.5%) in intravaginal insert group needed extra drugs for shortening the labour. In the study only two patients received epidural analgesia which was statistically insignificant. In intracervical gel group 46 patients (92%) needed extra drugs out of 50 patients delivered normally. Inspite of giving more oxytocin and more drugs for shortening labour the induction delivery interval was longer for intracervical gel group.

The birth weight is not a dependent factor for successful vaginal delivery according to this study. The mean birth weights were 3096.5 +/-371.4 grams and 3133.4 +/- 392.4 grams respectively. The p value was 0.599.

There was no statistically significant difference in the APGAR score of the newborn at 5 and 10 minutes of birth with a p value of 0.227 at 5 minutes of birth and 0.384 at 10 minutes of birth. There were 6 babies with APGAR of <7 at 5 minutes in intracervical gel group irrespective of the mode of delivery. There were 4 babies in intravaginal insert group with Apgar score <7 at 5 minutes irrespective of the mode of delivery.

Out of 120 deliveries 7 babies went to NICU for observation or intervention. 4 babies were from intracervical gel group and 3 babies were from intravaginal insert group. Hence there was no significant difference in the NICU admission of newborns between 2 groups.

There was no statistical difference between patient satisfactions which was assessed on the day of discharge of the patient. 47 patients in intracervical gel group told that they were satisfied with the induction method whereas 13 patients were found to be unsatisfied due to increased number of doses, number of per vaginal examinations, pain during active labour, prolonged labour, the caesarean section rate, the use of extra drugs and the need for longer stay.50 patients were satisfied out of 60 patients whom we used intravaginal insert whereas 10 patients were unsatisfied due to the anxiety of a new drug and hyperstimulation rate. It was found that reduced number of doses and number of per vaginal examination, shorter duration of labour without any addition of oxytocin and cervical dilators added points to the satisfaction for the patients in intravaginal insert group.

Labour is an emotional experience and involves both physiological and psychological mechanisms. Labour pain is ranked high on the pain rating scale when compared to other painful experiences. Labour pain has two components, visceral pain which occurs during the early first stage and second stage of child birth and somatic pain which occurs during the late first stage and second stage. The labour pain in the first stage is mediated by T10 to L1 spinal segments, whereas that in the second stage is carried by T12 to L1, and S2 to S4 spinal segments [20]. The pain during active labour was seen significantly higher with intracervical gel when compared with

intravaginal insert with a p value of <0.001. The pain was assessed with visual analogue scoring during the initial 6 hours of active labour.38 patients out 60 patients in intravaginal insert group had pains with VAS scoring of < 5 and 22 had score >5. It was noted that the pain was perceived more with intracervical gel with VAS score of >5 for 45 patients out of 60 subjects.

As observers for the study we found the administration and removal of the drugs were easier with dinoprostone vaginal insert, although monitoring was needed cautiously as hyperstimulation was seen more with it.

## Conclusion

Dinoprostone intravaginal insert was found to be more efficacious than intracervical gel (p value<0.001). Cervical ripening was significantly faster with intravaginal insert when compared with intracervical gel (p value<0.001). Induction delivery interval was significantly lower in dinoprostone vaginal insert group than with intracervical gel (p value<0.001) with shortening of active phase of labour to few minutes (p value<0.001). Very few patients with dinoprostone vaginal insert received oxytocin for augmentation of labour (p value<0.001). The use of labour analgesics and pharmacological cervical dilators were less for patients who were induced with intravaginal insert (p value<0.001). Both dinoprostone vaginal insert and intracervical gel are safe methods of induction of labour. Caesarean section rate (p value-0.803), incidence of meconium stained liquor (p value- 0.729), incidence of PPH (p value-0.648) did not show any significant difference between the two agents. Even though the incidence of hyperstimulation was more with vaginal insert it was not statistically significant (p value-0.240). APGAR scores at 5 minutes and 10 minutes (p value -0.227 and 0.389) and NICU admissions (p value -0.697) of the neonates did not show any significant difference between two groups.

Dinoprostone vaginal insert reduced number of vaginal examinations and thus reducing the chances of ascending infections. It also improved the comfortability of the patients as the intensity of the pain perceived after active labour ensued was less (p value-<0.001)

Dinoprostone vaginal insert was found to be satisfying for the obstetrician too due to the easier application and removal of the drug. Intravaginal insert also allows to start oxytocin infusion as early as 30minutes after the removal of the drug when compared with intracervical gel where we have to wait for 6 hours after the last application although the use of oxytocin infusion is lesser with intravaginal insert.

However with all these advantages, most of the Indian patients will find it difficult to buy intravaginal insert because of the cost factor. When analyzed, the cost effectiveness is found to be higher with intravaginal insert as the hospital stay is reduced because of the shorter induction delivery interval, less intensity of pain during initial hours of labour and less use of drugs for acceleration of labour or dilation of cervix.

Women should be counseled regarding the advantages and disadvantages of both the induction methods in conjunction with the cost effectiveness. Hence the method of induction should be individualized on the basis of affordability and patient acceptability.

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