

Analysis of Prostaglandins (Pge1 and Pge2) in Induction of Labour

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Abstract

Introduction: According to the definition by World Health Organization normal labour as “spontaneous in onset, low risk at the start of labour and remaining so throughout labour and delivery. Induction of labour is the non spontaneous initiation of uterine contractions that result in progressive cervical effacement and dilatation with descent of the presenting part to achieve vaginal delivery. The method of administration that has been explored thoroughly is PGE2 i.e, cerviprime gel. Though this is widely used, it is expensive and requires refrigeration for storage. The second method of administration used is Misoprostol or PGE1 tablets which is comparably cheap, safe and cost effective.

Aim and Objective: In the present study, our traditional methods of cervical ripening with endocervical prostaglandin E2 gel, and intravaginal prostaglandins PGE1 was used, to know the outcome after using these two drugs.

Material and Methods: The present Prospective Observational study was conducted in a Tertiary Care hospital during October 2015 to October 2017 amongst 100 patients admitted in labor room with following indication, Induction of labor in women at or beyond term, Induction of labor in women with pre-labor rupture of membranes, IUGR with or without Oligohydrominos, I.U.F.D and Hypertensive disorder of pregnancy. For induction, Misoprostol was used in 26 patients and Dinoprostone (cerviprime)

was used in 74 patients. Obstetrician were free to use their choice of drugs, between two, we have observed that Dinoprostone was more commonly used.

Result: Percentage of induction was more in Primigravida, but parity wise it was comparable. Dinoprostone used slightly more in Primigravida. It was found that irrespective of bishop score vaginal delivery was found to be more. Overall vaginal delivery with misoprostol group was more. It is statistically significant. The time required for delivery with misoprostol is less as compared with Dinoprostone which is statistically significant. It was found that induction done with Tab. Misoprostol has the highest vaginal delivery rate with 1 or 2 doses, and in Dinoprostone maximum 3 doses were required. 11.3% required LSCS for foetal distress and around 17% of patients landed up in failure of induction. None of the misoprostol group had failure of Induction. No any complications were found like hypertonus, tachysystole, and rupture of uterus.

Conclusion: From the present study it was concluded that PGE2 (Dinoprostone) and PGE1 (Misoprostol) are equally safe, Obstetrician was free to use their choice of drugs, and we have observed that Dinoprostone was commonly used. Considering its safety it is observed that both are equally safe, but the cost effectiveness of misoprostol is more, which may be the drug of choice in coming years.

Keywords: Prostaglandins; Misoprostol; Dinoprostone; Cerviprime; Induction.

Introduction

The World Health Organization defines normal labour as “spontaneous in onset, low risk at the start of labour and remaining so throughout labour and delivery.¹ The infant is born spontaneously in the vertex position between 37 and 42 completed weeks of pregnancy. Induction of labour is the non spontaneous initiation of uterine contractions that result in progressive cervical effacement and dilatation with descent of the presenting part to achieve vaginal delivery. In order to be successful, induction of labour there must be under three criteria. First, it should result in labour with adequate uterine contractions and progressive dilatation of the cervix, secondly it should undergo vaginal delivery, and lastly minimal risk to both mother and foetus.

The method of administration that has been explored thoroughly is PGE2 i.e, cerviprime gel.

Though this is widely used, it is expensive and requires refrigeration for storage. The second method of administration used is Misoprostol or PGE1 tablets which is comparably cheap, safe and cost effective.

In the present study, our traditional methods of cervical ripening with endocervical prostaglandin E2 gel, and intravaginal prostaglandins PGE1 was used, to know the outcome after using these two drugs.

We have undertaken this study because:

- The incidence of induction of labour with PGE2 is 28.4% in our hospital.
- PGE1 analogue is equally effective but not used in our institute regularly so we are going to do this study so that a new protocol can be set in our department regarding use of PGE1 and PGE2.

Aim

To study the role of prostaglandins in induction of labour.

Objectives

To study the outcome of labour in patients induced with Prostaglandins.

- Outcome of delivery in association with Bishop score.

Material and Methods

Study Centre: Tertiary Care hospital

Study Period: October 2015 to October 2017.

Type of study: Prospective Observational study.

Sample size: 100

Inclusion Criteria

All patients admitted in labor room with following indications:

- i. Induction of labor in women at or beyond term.
- ii. Induction of labor in women with pre-labor rupture of membranes.
- iii. IUGR with or without Oligohydrominos.
- iv. I.U.F.D
- v. Hypertensive disorder of pregnancy.

Exclusion Criteria

- i. Combined method used for induction. e.g cerviprime gel done with intracervical foleys. In the present study 100 patients were enrolled, those who gave consent for the study and in whom labour induction was indicated. In these 26 patients underwent induction with Tab. Misoprostol in the posterior vaginal fornix, 74 patients underwent induction with Dinoprostone with 0.5mg half in posterior vaginal fornix and half intracervical.

Statistical Analysis

Data was entered into Microsoft excel data sheet and was analyzed using SPSS 22 version software. Categorical data was represented in the form of Frequencies and proportions. Chi square test was used as test of significance for qualitative data.

Graphical representation of data: MS Excel and MS word was used to obtain various types of graphs such as bar diagram and Pie diagram.

p value (Probability that the result is true) of <0.05 was considered as statistically significant after assuming all the rules of statistical tests.

In the present study no. of patients enrolled were 100.

Misoprostol was used in 26 patients and Dinoprostone (cerviprime) was used in 74 patients.

Obstetrician were free to use their choice of drugs, between two, we have observed that Dinoprostone was more commonly used.

Results

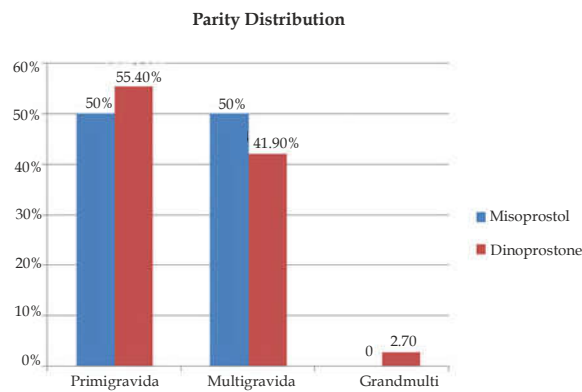


Fig. 1: Bar diagram showing Parity distribution in the analysis of the two methods used:

$$\chi^2 = 1.094, df = 2, p = 0.579$$

Fig. 1, Percentage of induction was more in Primigravida, but parity wise it was comparable. Dinoprostone used slightly more in Primigravida.

Table 1(A): Outcome of delivery in association with Bishop score in Misoprostol group

N- 26 Cases	Vaginal Delivery	Caesarean
Bishop 6 -7	15(93.75%)	1(6.25%)
Bishop > 8	10(100%)	0
Total	25	1

P value = 0.0001 it was statistically significant

Table 1 (B): Outcome of delivery in association with Bishop score in Cerviprime Group:

N- 74 Cases	Vaginal Delivery	Caesarean
Bishop 6 -7	37(72.54%)	14(27.54%)
Bishop > 8	21(91.30%)	2(8.6%)
Total	58	16

P value=0.05 it was statistically significant.

It was found that irrespective of bishop score vaginal delivery was found to be more. Overall vaginal delivery with misoprostol group was more. It is statistically significant.

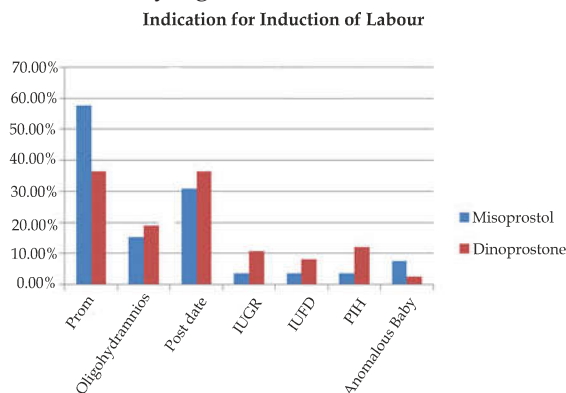


Fig. 2: Bar diagram showing Analysis of Indications for induction of Labour in the two methods.

From the fig. 2, it signifies that in cerviprime gel the maximum indication used was PROM and postdatism. In misoprostol group, PROM was the commonest indication.

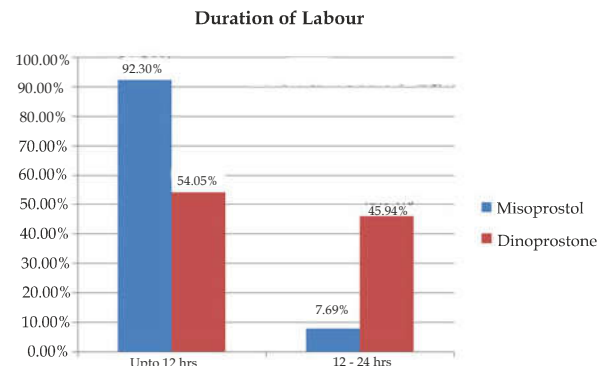


Fig. 3: Bar diagram showing Duration of labour in analysis of the two methods used.

p value= 0.005 it is significant. $\chi^2 = 10.61, df = 2$

From the fig. 3, it signifies that time required for delivery with misoprostol is less as compared with Dinoprostone which is statistically significant.

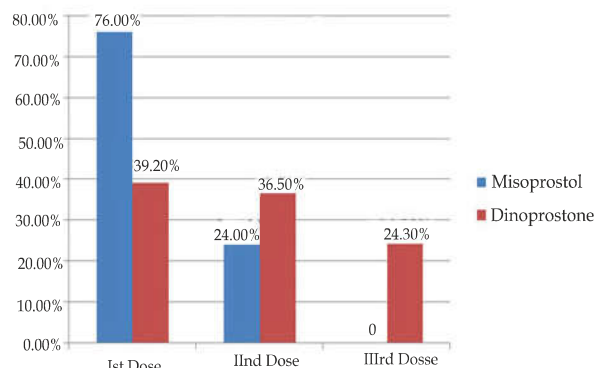


Fig. 4: Bar diagram showing no. of doses of cerviprime and misoprostol in analysis between two methods used.

P value = 0.005 it is significant.

From the Fig. 4, it is found that induction done with Tab. Misoprostol has the highest vaginal delivery rate with 1 or 2 doses, and in Dinoprostone maximum 3 doses were required.

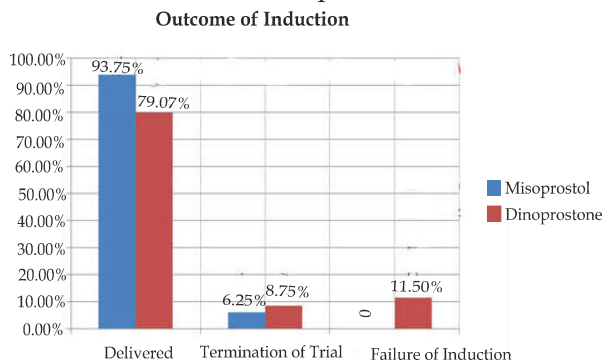


Fig. 5: Bar diagram showing Outcome of induction in analysis of two methods.

$$\chi^2 = 0.752, df = 2, p = 0.686$$

Fig. 5, indicates that 11.3% required LSCS for foetal distress and around 17% of patients landed up in failure of induction. None of the misoprostol group had failure of Induction. No any complications were found like hypertonus, tachysystole, and rupture of uterus.

Discussion

In the present study 100 patients were enrolled. Misoprostol was used in 26 patients and Dinoprostone (cerviprime) was used in 74 patients.

Prostaglandins

Prostaglandins are the important factors which initiate and maintain labor. The major sites of synthesis of prostaglandins are- amnion, chorion, decidual cells and myometrium. Synthesis is triggered by-rise in estrogen level, glucocorticoids, mechanical stretching in late pregnancy, increase in cytokines (IL-1,6,TNF), Infection,vaginal examination, separation or rupture of membrane. Prostaglandins enhance gap junction (intermembranous gap between two cells through which stimulus flows) formation. Labor is a stress factor for the fetus. During active labor the integrity of the uteroplacental circulation and the frequency and intensity of uterine activity influence the acid base status of the fetus which is reflected in the fetal heart tracings on cardiotocograph. Fetal heart rate monitoring is sensitive sufficient to diagnose fetal asphyxia before permanent brain damage occurs.

Induction of labor means initiation of uterine contraction (after the period of viability) by any method (medical, surgical, mechanical or combined) for the purpose of vaginal delivery. Prostaglandins can also be used as an abortifacient. It is a direct vasodilator, relaxing smooth muscles, and it inhibits the release of adrenaline from sympathetic nerve terminals. It works by binding and activating the prostaglandin E2 receptor. Prostaglandins came in existence in 1960. It was discovered by Bunting, Gryglewski, Moncada and Vane in 1976. (prostaglandins E2). Prostaglandins are capable of stimulating uterine contractions resulting in labour. Prostaglandins can be administered by various routes: vaginal, oral, intravenous, extra amniotic, and intracervical.

Vaginal Pge2²³

The vaginal preparations of PGE2 are used in the form of tables, pessary, and suppository. In women with unfavorable cervix, all regimens of

vaginal PGE2 are significantly associated with uterine hyper stimulation with fetal heart rate (FHR) changes, improved cervical status within 24 hours, and reduction in the need for oxytocin augmentation and reduced incidence of meconium-stained liquor. In women with a favorable cervix, all regimens of vaginal PGE2 are more effective than placebo.

Misoprostol

Misoprostol is a synthetic prostaglandin that can be orally, vaginally, sublingually. It is effective in causing uterine contractions .misoprostol usually comes in tablets of 25, 50, 100 and 200 micrograms.

Vaginal Misoprostol^{4,5}

Evidence suggested that, for women with an unfavorable cervix, vaginal misoprostol is more effective than placebo as an inducing agent .vaginal misoprostol (25-50microgram) is more likely than vaginal PGE2 to produce a favorable cervix within 24 hours, achieve birth within 24 hours, and cause uterine hyper stimulation without foetal heart rate changes. Vaginal misoprostol at lower dose (minimum 25 microgram) was is more likely than high dose (maximum 50microgram) to cause uterine hyper stimulation with and without FHR changes. Vaginal misoprostol is more likely than Isosorbide Mononitrate to achieve birth and not need oxytocin augmentation. Tachysystole and uterine hyper stimulation are less likely in women given vaginal isosorbide mononitrate. There were more reports of headaches, nausea, and dizziness in the isosorbide mononitrate.

1. Age of the Patients

It was found that maximum patients for induction were in the age group of 19-35 (97.30%) of years. Distribution of patients in both the groups was comparable. In a study done by S.Kulshreshtha, P.Sharma, G.Mohan⁶ in 2007 they also found about 90% of the patients were in the age group of 19-35 years.

2. Parity of the Patients

In the present study, percentage of Induction was more in Primigravida. Dinoprostone was used more in Primigravida. Study done by Luis Sanchez Ramos et. al.⁷ in 1998, the induction was more in multigravida, with misoprostol it was 62% and 55% with Dinoprostone, but in my study primigravida forms a larger group.

3. Booking Status

It was found that majority of patients were in unbooked group i.e, 63%. The patient in unbooked

group had no regular antenatal checkups. Need for induction was more in unbooked patients, as they are having more complications related with pregnancy. Study done by G.K Pandis, K.H Nicolaidis⁸ in 2001 they also found that due to irregular visits more patients were in unbooked group i.e 65%.

4. Gestational age at Induction

In the present study it was found that 57.70% in misoprostol and 47.30% in Dinoprostone at the term were induced. In majority cases Oligohydrominos and IUGR were indications. Choice of drug was Misoprostol at term and Dinoprostone gel at post datism. In the preterm it was observed that 15.40% in misoprostol and 17.60% in Dinoprostone gel group the maximum indication were hypertensive disorder in pregnancy, oligohydrominos. It was found that preterm induction was less. The study was consistent with Trufatter et. al.⁹ in 1985 they also observed that preterm induction was less.

5. Mode of Delivery

The rate of vaginal deliveries was 92.3% in the misoprostol group and 79.70% in the Dinoprostone group. The vaginal delivery rate with Misoprostol in present study is consistent with the studies of Luis Sanchez Ramos et. al.⁷ in 1998 which was 90.7%. Bugalho et. al.¹⁰ in 1995 which was 92.2%. In the present study, the rate of vaginal deliveries in the Dinoprostone group is consistent with the studies of Trufatter et. al.⁹ in 1985 it was 73.3% and Nager et. al.¹¹ in 1987 which was 73.7%. Rest of patients i.e, 27% delivered by operative i.e LSCS and instrumental.

6. Bishop Score

In the present study it was found that the in both the groups, Bishop Score more than 8 has highest percentage of outcome of deliveries, in misoprostol it was 100% and in Dinoprostone it was 91.30%. It was found that irrespective of Bishop Score vaginal delivery was found to be more. Present study is consistent with S.Katherine Laughon, JUN Zhang¹² in 2011 that irrespective Bishop score vaginal delivery was found to be more.

7. Indications for Induction

In the present study it was found that about 57.70% cases in misoprostol group was induced due to PROM, and in Dinoprostone group 36.50% cases were induced. Oligohydrominos- In misoprostol group it was 15.40% and in Dinoprostone it was 18.90%. Post Datism- In misoprostol group it was 30.80% and in Dinoprostone it was 36.50%.

IUGR- In misoprostol group it was 3.80% and in Dinoprostone group it was 10.80%. Use of Dinoprostone was slightly more in IUGR patients. Diagnosed IUFD- In misoprostol group it was 3.80%, and in Dinoprostone group it was 8.10%. PIH- In misoprostol group it was 3.80% and in Dinoprostone group it was 12.20%.

Anomalous Baby: In misoprostol group it was 7.70% and in Dinoprostone group it was 2.70%.

It was comparable with the studies of Trufatter et. al.⁹ in 1985 he observed that maximum indication required for misoprostol was PROM, i.e, 65%. In Dinoprostone group maximum indication was postdatism, i.e 52%.

8. Induction to Delivery Interval

In the present study it was seen that the induction delivery interval was shorter in misoprostol group compared to Dinoprostone group. In misoprostol group upto 12 hours it was 92.30% and in Dinoprostone group it was 54.05%. In the second group, in 12 to 24 hours 7.69% was in misoprostol group and 27% in cerviprime group. It was comparable with the studies of Trufatter et. al.⁹ in 1985 and Yonekur et. al.¹³ in 1985, and was found that induction delivery interval was shorter in misoprostol group than with Dinoprostone group.

9. Number of Doses of Misoprostol and Cerviprime in the Two Methods Used

In the 1st group it was decided to use Tab. Misoprostol 25µg 4 hourly for 3 doses. It was observed that 76% delivered with 1st dose of misoprostol and with 2nd dose it was 24.00%, 3rd dose was not required. It is comparable with the studies of Wing et. al.¹⁴ in 1995 who has used 25µg in single or repeated dose and the outcome was found same. The other study was done by Sanchez Ramos et. al.⁷ in 1993 has used 50µg misoprostol which was used in single or repeated dose, the outcome of delivery was similar.

In the Dinoprostone group no. of doses used were 3 doses 0.5mg which was repeated every 6 hourly, It was observed that 39.20% delivered in 1st Dinoprostone, 36.50% delivered in 2nd gel, 35.10% delivered in 3rd gel. It was comparable to the studies with Ozgur et. al.¹⁵ in 1997.

10. Outcome of Induction

The first complication observed was failure of induction which resulted in LSCS. In the present study caesarean rate was 7.70% in misoprostol group and in Dinoprostone group it was 17.60%. The indications were fetal distress, failure to induction,

no other complications were found like rupture of uterus. In Misoprostol group the rate of caesarean delivery was 7.70% which is comparable with the study done by Sanchez Ramos⁷ in 1997 they found that in 9.8% of women had undergone caesarean section due to foetal distress.

In our study the caesarean section rate with Dinoprostone was 17.60% which was comparable with the studies done by NAGER et. al.¹¹ in 1987 he found that in Dinoprostone group there was 26.3% caesarean rate which was due to failure of induction. And the same study was done by Bernstein et. al.¹⁶ in 2005 he also found that there was 30.8% caesarean in Dinoprostone.

Maternal Side Effects

In the present study it was observed that there was no side effects to the mother like tachysystole, hyper stimulation, hypertonus, PPH, vomiting, fever, diarrhoea in neither of the two groups.

11. Neonatal Outcome

It was observed that 85% of the babies were with mother. 3.80% babies in misoprostol group required NICU admission and in Dinoprostone group 5.40% babies required NICU admission. The indications of NICU admission were neonates having low birth weight, prematurity, and birth asphyxia. In a study by Mundle and Young¹⁷ in 1996 studied that effect of misoprostol and cerviprime in labour induction on neonatal outcome has similar effects in both the groups.

12. Oxytocin Augmentation

Oxytocin was started depending on the modified Bishop score. In the present study it was observed that oxytocin required in very minimal patients. It was comparable in both the groups. The study done by Wing DA et. al.¹⁴ in 1999, requirement of oxytocin in misoprostol is more in this study, this may be the difference in doses. Overall it is observed that in the 1st group, maximum 1 or 2 doses of misoprostol are required to achieve the outcome of induction, and while in the 2nd group 2 or 3 gels are required upto delivery to achieve the outcome. It was observed that a single dose of Dinoprostone costs Rs. 240 and upto 3 gel the maximum costs was Rs.580. A single dose of misoprostol costs Rs 7 and pack of 4 costs upto 48. Thus concluding that misoprostol is more cost effective and easy storage than Dinoprostone, as Dinoprostone needs to be stored in the refrigerator between 2 to 8 degree Celsius.

Summary and Conclusions

In the present study 100 patients were enrolled who had given consent for the study and in whom labour induction was indicated. In these 26 patients underwent induction with Tab. Misoprostol in the posterior vaginal fornix, 74 patients underwent induction with Dinoprostone with 0.5mg half in posterior vaginal fornix and half intracervical.

1. In the misoprostol group it is 92.30%, and Dinoprostone group 97.30% were in reproductive age group 19-35.
2. 55.40% patient's undergone induction with Dinoprostone in Primigravida, 50% in Misoprostol. 41.90% in multigravida with cerviprime and 50.00% in Misoprostol.
3. In the Dinoprostone group, 43.30% were booked and 56.70% were unbooked. In misoprostol group, 61.50% were unbooked and 38.50% were booked.
4. In Dinoprostone group, 47.30% has undergone induction in Term pregnancy, and 57.70% in Misoprostol group. 35.10% has undergone induction with cerviprime in Post term pregnancy and 26.90% in Misoprostol. Preterm induction was less in my study.
5. In my study vaginal delivery forms the largest group. 79.70% in Dinoprostone group undergone vaginal delivery, 92.30% in Misoprostol. 17.60% has undergone caesarean in cerviprime group, and 7.70% in Misoprostol. Instrumental delivery was seen in i.e 2.70% in Dinoprostone group.
6. 100% of patient in Misoprostol group with Bishop score more than 8 has delivered vaginally, and in Bishop score 6-7, 93.75% has delivered vaginally and only 6.25% has underwent LSCS. 91.30% of patients in Dinoprostone group with Bishop score more than 8 has delivered vaginally, and 8.6% has underwent LSCS. 72.54% in Dinoprostone group with Bishop score 6-7 has delivered vaginally, and 27.54% has underwent LSCS.
7. In misoprostol group 57.70% had induction with indication of PROM, 15.40% in Oligohydrominos, 30.80% in Postdatism, 3.80% in IUGR, 3.38% in IUFD, 3.80% in PIH, 7.70% in Anomalous baby. In Dinoprostone group 36.50% has underwent induction with indication with PROM, 18.90% in OLIGO, 36.50% in Paostdatism, 10.80% in IUGR, 8.10% in IUFD, 12.20% in PIH, and 2.70% in Anomalous Baby.

8. In my study i found that 92.30% in misoprostol group and 54.05% in Dinoprostone group delivered upto 12 hours. In 7.69% in misoprostol group and 27.00% in Dinoprostone group delivered in 12 to 24 hours.
9. In Dinoprostone group, 39.20% required one dose of gel, 36.50% required 2nd dose of gel, 35.10% required 3rd gel. In misoprostol group, 76% required only one dose of misoprostol, and 24% required 2nd dose of misoprostol.
10. Oxytocin augmentation required is very minimal in Patients. It was comparable in both the group.
11. The rate of failed induction was 11.50% in Dinoprostone group, and 8.15% in misoprostol group, the reason is failure of induction, 8.10% in cerviprime group some went termination of trial and 3.80% in misoprostol group the reason may be foetal distress. There was only 9% incidence of NICU admission in both groups. 85% were baby with mother.

From the above summary it was concluded that

Literature says that PGE2(Dinoprostone) is more safe than PGE1 (Misoprostol). The present study shows that it is equally safe, Obstetrician was free to use their choice of drugs, and we have observed that Dinoprostone was commonly used. Considering its safety it is observed that both are equally safe, but the cost effectiveness of misoprostol is more, which may be the drug of choice in coming years.

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