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Original Research Article

To compare the effects of intra vaginal prostaglandin E1 and intra-cervical prostaglandin E2 for prelabour ripening of unfavorable uterine cervix in nulliparous women

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ABSTRACT

Background: Induction of labour by use of prostaglandins improves the obstetric outcome in complicated cases such as prolonged deliveries. The aim of the present study was to compare the effect of prostaglandin E1 (PGE1) and prostaglandin E2 (PGE2) for prelabour ripening of unfavourable uterine cervix in nulliparous women, to study the effect of PGE1 and PGE2 on duration of labor and to evaluate the obstetrical and neonatal outcome of induction of labour using prostaglandins E1 and E2.

Methods: This was a prospective study conducted on 50 nulliparous women with singleton pregnancy with gestational age ≥37 weeks during the period from August 2008 to October 2010 in the Department of Obstetrics and Gynaecology of Bombay Hospital Institute of Medical Sciences and Allied Hospitals, Mumbai. All the 50 patients were divided into two groups. Group-1 containing 25 patients received intravaginal PGE1, (Tablet Misoprostol 25 mcg) inserted in the posterior vaginal fornix under all aseptic precautions. Group-2 containing 25 patients received intracervical PGE2, (Dinoprostone gel, 0.5 mg). Analysis and comparison of various parameters like induction-delivery interval, Bishops score before and after administration of drug, mode of delivery, neonatal outcome, foeto-maternal complications between the two groups were noted and analysed the data statistically by using Chi-square, continuity correction, Fisher's exact test and Mann-Whitney tests.

Results: Majority of the patients in both the groups were under the age of 23-27 years. Post-datism was the common indication noticed in 18 (72%) and 13 (52%) patients of both the groups respectively. Maximum patients had a Bishop's score of 3 in PGE1 (56%) and PGE2 groups (48%) respectively. The improvement in Bishop's score in both the groups before and after drug administration was 6.20 and 6.76 respectively. Maximum patients in both the groups went into active labour within six hours of induction of labour. The most common side effects seen in our study was nausea and vomiting in both groups. Majority (23) were born with Apgar score 8-10 in group 1 and 21 for group 2 patients.

Conclusions: Both the drugs had similar efficacy and safety in induction of labour. Prospective research is required to fully evaluate the impact of AMOR-IPAT on nulliparous birth outcomes.

Keywords: Intravaginal PGE1, Intracervical PGE2, Nulliparous women, Uterine cervix

INTRODUCTION

In order to reduce the risk of maternal or neonatal morbidity and mortality, labour is often induced.[1] According to WHO global survey reports, 9.6% of cases out of 3 lakhs population were delivered by labor induction.[2]

Prostaglandins are widely used in clinical practice since 1960s for induction of labour but side-effects such as

gastrointestinal symptoms (nausea, diarrhoea, and vomiting), uterine hyper stimulation, and fever are reported.[3-5] Dinoprostone is the widely used prostaglandin E2 analogue that has been approved by the FDA for cervical ripening in women. In many centers misoprostol, the prostaglandin E1 analogue, has replaced the use of dinoprostone due to its lower cost, higher stability and probably higher efficacy.[6]

The present study was undertaken with the aim to compare the effect of prostaglandin E1 and prostaglandin E2 for prelabour ripening of unfavourable uterine cervix in nulliparous women, to study the effect of prostaglandin E1 and prostaglandin E2 on duration of labour and to evaluate the obstetrical and neonatal outcome of induction of labour using prostaglandins E1 and E2.

METHODS

This prospective cohort study was conducted for a period of two years from August 2008 to October 2010 in the Department of Obstetrics and Gynaecology of Bombay Hospital Institute of Medical Sciences and Allied Hospitals, Mumbai. Total numbers of cases were fifty and they were divided into two equal groups. All registered nulliparous women with singleton pregnancy with gestational age ≥37 weeks were randomly assigned by simple random sample selection method to two groups each containing 25 patients. An approval was taken for conducting this study from local ethics committee and scientific research society.

Inclusion criteria included nulliparous women with singleton pregnancy with gestational age ≥37 weeks, Bishop's score of ≤4, cephalic presentation of foetus and medical or obstetric reason for induction of labour

Exclusion criteria were evidence of cephalopelvic disproportion on vaginal examination, multigravida women, presence of malpresentations, multiple pregnancies, fetal heart rate abnormality documented by admission non stress test, prelabour rupture of membranes, any vaginal bleeding, history of previous surgery on uterus, hypersensitivity to prostaglandins or any medical conditions precluding use of prostaglandins, history of previous surgery on cervix , cervical carcinoma, pelvi tumours and presence of active herpetic genital lesions

Written informed consent was taken from all the patients before the study. Detailed history was taken which included menstrual, obstetric and relevant past medical or surgical history. Calculation of gestational age was done by last menstrual period and first trimester ultrasound. A routine per abdominal examination was done to confirm gestational age, presentation, adequacy of liquor and fetal heart sound.

Detailed pelvic examination was done to judge the condition of cervix according to Bishop's score and adequacy of pelvis. An admission fetal non-stress test was carried out to asses' fetal wellbeing. The patients with reactive NST were taken for the study.

General and systemic examination (cardiovascular system and respiratory system) was also performed. All biochemical investigations including blood and urine examinations were done. Baseline parameters were noted. Pre-induction counselling was done. Patients were explained about the need for induction as well as use of the drugs, their safety and adverse effects.

Shaving of the perineal area was done. Bishop's score was noted prior to induction (at zero hour). Patients were not starved and were ambulatory and were allowed to take light diet. A non-stress test was done for 10 minutes prior to induction to assess the baseline fetal condition. When non-stress test was reactive, patient was induced with either of the 2 drugs. Patients were assigned to any of the two methods viz, induction with intravaginal prostaglandin E125 mcg and intracervical prostaglandin E2 gel 0.5 mg.

Method of induction and drugs-dosage regimen

All the 50 patients were divided into two groups. Group-1 containing 25 patients received intravaginal prostaglandin E1 (PGE1), (Tablet Misoprostol 25 mcg) inserted in the posterior vaginal fornix under all aseptic precautions.

Group-2 containing 25 patients received intracervical prostaglandin E2 (PGE2), (Dinoprostone gel, 0.5 mg). Patient was given lithotomy position. After local preparation in good light, under direct visualisation of cervix, a prefilled syringe with an inserter was introduced through the cervical canal up to the level of internal os. Under all aseptic precautions, the gel was slowly injected with simultaneously withdrawing the applicator. The patient was asked to remain in supine position for half an hour after which she was asked to ambulate.

All patients, vital parameters were recorded and per abdomen examination was done one hourly for uterine activity, tachysystole or hyperstimulation. Fetal heart rate was monitored. All patients were reassessed after 6 hours (at 6 hours) and re-induction with same method was done if required. Reassessment was done to note improvement in Bishop's score and progression to active phase.

The re-induction patients were reassessed after 6 hours again (at 12 hours) and were labelled failed induction if Bishop's score was less than 6, failure to enter the active phase of labour (uterine contractions causing progressive cervical dilatation and effacement).[7]

No further doses were given if there were uterine contractions, if membranes ruptured spontaneously or if there were any fetal heart rate abnormalities. Oxytocin was used for augmentation of labour subsequent to

artificial rupture of the membranes, according to departmental protocols.

Throughout the labour partogram was maintained and progress of labour was monitored. The detailed analysis was carried out for both groups regarding: Improvement in Bishop's score at six hours and twelve hours, percentage of patients who end in labour following induction at assigned intervals, mode of delivery, number of patients requiring caesarean section, induction delivery interval, incidence of uterine hyperstimulation / tachysystole, drug related side effects and perinatal outcome with respect to Apgar score at birth

Uterine tachysystole was defined as six or more contractions in any 10-minute period, and hyperstimulation as fetal heart rate abnormality associated with tachysystole. Tachysystole and hyperstimulation were determined from a standard cardiotocogram.

Statistical analysis

Statistical analysis of the results was carried out with Chi-square (Pearson Chi-Square), continuity correction, Fisher's exact test and Mann-Whitney tests to compare the effects of intravaginal prostaglandin E1 and intracervical prostaglandin E2 gel for prelabour ripening of unfavourable cervix in term nulliparous women.

RESULTS

Patients of age group above 18 years were included in the study. Majority of the patients in both the groups were under the age of 23-27 years as shown in Table 1.

Table 1: Age distribution of patients.

Age (years)	Groups n (%)		Total (n=50)
	PGE1 (n=25)	PGE2 (n=25)	
18 to 22	4 (16)	6 (24)	10 (20)
23 to 27	11 (44)	13 (52)	24 (48)
28 to 33	10 (40)	4 (16)	14 (28)
≥ 33	0 (0)	2 (8)	2 (4)

Table 2: Indication of induction of labour among both the groups.

Indications	Groups n (%)	
	PGE1 (n=25)	PGE2 (n=25)
Post-datism	18 (72)	13 (52)
Elective	4 (16)	4 (16)
PIH	2 (8)	5 (20)
GDM	0 (0)	2 (8)
ITP	1 (4)	0 (0)
IUFD	0 (0)	1 (4)

Post-datism was the common indication noticed in 18 (72%) and 13 (52%) patients of both the groups respectively as given in Table 2. Bishop's score in the patients of the both the groups were presented in Table 3. No patient had a score of 0 in either group. Maximum patients had a Bishop's score of 3 in PGE1 (56%) and PGE2 groups (48%) respectively.

Table 3: Analysis of preinduction Bishop's score in both groups.

Bishop's score	Groups n (%)	
	PGE1 (n=25)	PGE2 (n=25)
0	0	0
1	2 (8)	1 (4)
2	9 (36)	11 (44)
3	14 (56)	12 (48)
4	0	1 (4)

Improvement in Bishop's score after administration of drugs in both the groups was shown in Figure 1. The mean initial Bishop's score (at o hour) in PGE1 group was 2.48 and in PGE2 group was 2.52. The mean post induction Bishop's score (at 6 hours) in PGE1 group was 8.68 and in PGE2 group was 9.28. The improvement in Bishop's score in both the groups was 6.20 and 6.76 respectively and was found no significant different in both the groups using Mann-Whitney test (p=0.9).

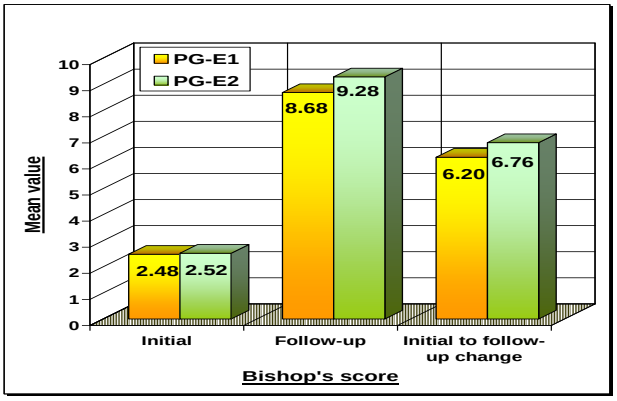

Figure 1: Improvement in Bishop's score in both the groups.

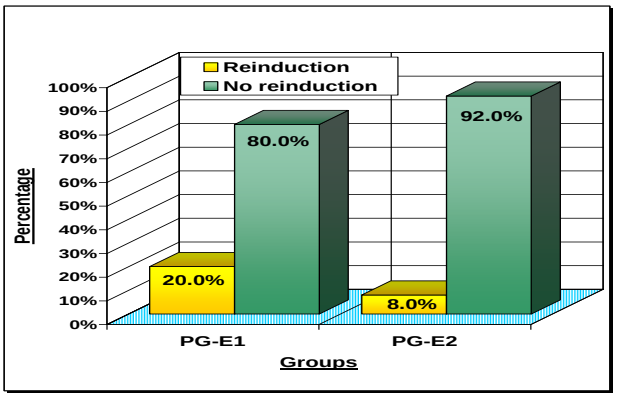

Figure 2: Total number of patients subjected to re-induction with the same agent.

Re-induction of PGE1 was given in 5 patients and PGE2 in 2 patients in respective groups. Out of 5 patients of PGE1 group, 4 patients required caesarean section and one delivered vaginally within 24 hours. Of 2 patients of PGE2 group, both delivered vaginally within 24 hours but one required vacuum assisted delivery in view of fetal distress as depicted in Figure 2.

Table 4: Analysis of time interval between induction of labour to onset of labour between the groups.

Induction to onset of labour interval (hours)	Groups n (%)	
	PGE1 (n=19)	PGE2 (n=22)
0 to 3	2 (10.5)	1 (4.5)
3 to 6	10 (52.6)	13 (59.1)
6 to 9	6 (31.6)	7 (31.8)
9 to 12	1 (5.3)	1 (4.5)

Maximum patients in PGE1 (63.15%) group and (63.6%) in PGE2 group went into active labour within six hours of induction of labour as given in Table 4. Delivery time in both the groups was presented in Figure 3. In group-1, 12 (63.2%) and in group 2, 14 (63.6%) were delivered within <12 hours of drug administration.

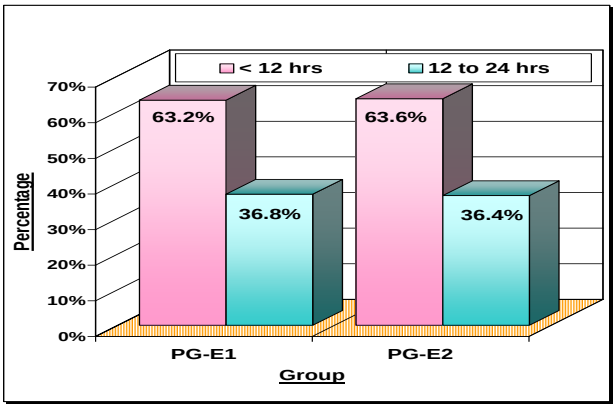

Figure 3: Analysis of time interval between induction of labour to vaginal delivery between the two groups.

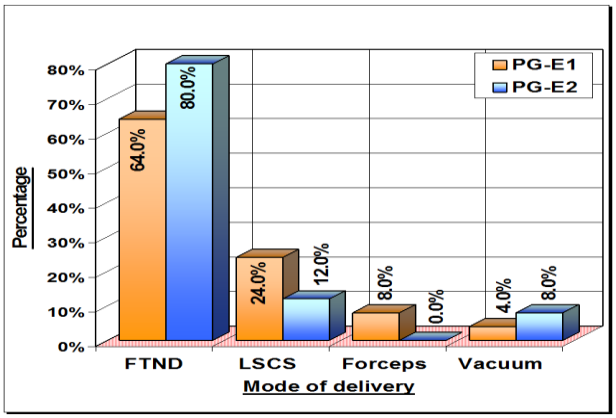

Figure 4: Various modes of delivery among the two groups.

Mode of delivery in both the groups was given in Figure 4. 19 (76%) and 22 (88%) patients of both groups delivered babies through vaginal route. Of them 16 (64%) and 20 (80%) patients of PGE1 and PGE2 groups had normal vaginal delivery. 3 (12%) patients in PGE1 group and 2 (8%) patients in PGE2 group required instrumental delivery in view of fetal distress (vacuum or forceps were used according to departmental protocols). Using Fisher's exact test (p=0.3), no significant difference was found between the two groups. 6 patients (24%) in PGE1 group and 3 patients (12%) in PGE2 group required caesarean section. Applying Pearson Chi -Square test (p=0.3), there is no statistically significant difference in caesarean section rate between both the methods of induction of labour.

Table 5: Indication of LSCS among prostaglandins E1 and E2 groups.

Indication of caesarean section	Groups n (%)	
	PGE1 (n=25)	PGE2 (n=25)
Failed induction	2 (8)	0
Fetal distress	2 (8)	1 (4)
Meconium stained amniotic fluid	2 (8)	1 (4)
Non-progress	0	1 (4)

Indications for LSCS in both the groups were given in Table 5. Fetal distress and meconium stained amniotic fluid were the common indications in both the groups seen in 2 (8%) and 1 (4%) patient in each group respectively.

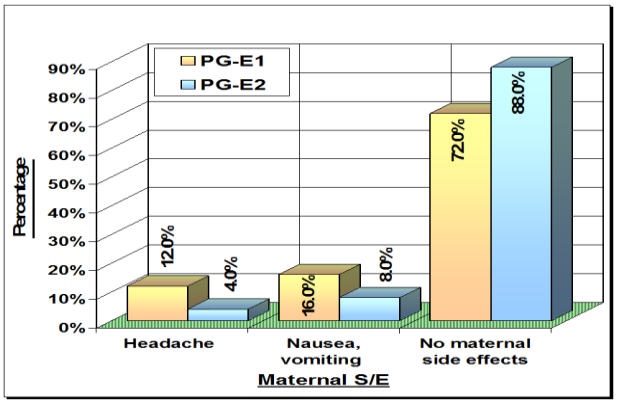

Figure 5: Side effects and complications observed with the use of induction agents.

The most common side effects seen in our study was nausea and vomiting in both groups. Incidence of uterine rupture, hyperstimulation or tachysystole was not observed in this study (Figure 5).

Analysis of Apgar score was done for all new born. All the babies born in PGE1 group had a higher Apgar score (7-10). One baby in PGE2 group had an Apgar score of 6, 7 and one born as macerated still birth (Table 6).

Table 6: Analysis of Apgar score.

Apgar score	Groups n (%)	
	PGE1 (n=25)	PGE2 (n=25)
9, 10	10 (40)	13 (52)
8, 9	13 (52)	8 (32)
7, 8	2 (8)	2 (8)
6, 7	0.0	1 (4)
MSB	0	1 (4)

2 (8%) babies in prostaglandin E1 and 1 (4%) baby in prostaglandin E2 group required to be admitted in neonatal intensive care unit. One baby of PGE2 group was admitted in NICU for 3 days due to poor Apgar score (6, 7). One baby of PGE1 group was having thick meconium stained amniotic fluid, and developed meconium aspiration syndrome, shifted to NICU for 3 days and started on antibiotics, supplementary oxygen. Another baby of PGE1 group had tachypnea, was admitted in NICU for 2 days and required supplementary oxygen. All babies recovered well and were discharged with no sequelae. There was no intrauterine fetal death or perinatal mortality due to our induction agents (Table 7).

Table 7: Need of NICU requirement in both the groups.

NICU Requirement	Groups n (%)	
	PGE1 (n=25)	PGE1 (n=25)
Yes	2 (8)	1 (4)
No	23 (92)	24 (96)

DISCUSSION

Induction of labour by use of prostaglandins is very common now-a-days. The reason for this is mainly due to a rise of inductions for marginal or elective reasons.[8,9] This prospective study was done to compare and evaluate the effects of intravaginal PGE1 versus intracervical PGE2 for prelabour ripening of unfavourable cervix in a term nulliparous woman.

In present study, majority of the women were in the age group of 23 to 27 years. The mean age of women in PGE1 group was 26.1 years and in PGE2 group was 25.1 years. This was comparable with the studies of Fletcher et al, involving sixty-three women comparing intravaginal PGE1 and E2, the mean gestational age was 39.1 weeks and 40 weeks respectively.[10] In this study, there were no demographic differences between the two groups. There were no post-randomisation exclusions, and no woman withdrew from the trial after consent had been given.

In our series, the mean initial Bishop's score in PGE1 group was 2.48 and in PGE2 group were 2.52. In a retrospective study analysing 81 patients by Blanchette et al, the mean pre-induction Bishop's score was 3.1 in PGE1 group and 2.9 in PGE2 group.[11] The mean post induction Bishop's score (at 6 hours) in our study in PGE1 group was 8.68 and in PGE2 group was 9.28. The improvement in Bishop's score was not significantly different in both the groups using Mann-Whitney test (p=0.9). 5 patients in PGE1 group and 2 patients in PGE2 group had to undergo re-induction, the difference being statistically not significant (p=0.2).

The most common indication for induction of labour in both the groups was post-datism (72% in PGE1 group and 52% in PGE2 group). Similar results were observed in the studies of Blanchetteet al and Calder et al.[11,12]

Time interval between induction to onset of labour was 310 min in PGE1 group and 336.1 min in PGE2 group. This difference was not found to be statistically significant. Similar observations were made by Calder et al.[12] In present study, more number of patients in PGE2 group (14) delivered in <12 hours as compared to prostaglandin E1 group (12). 7 patients in prostaglandin E1 group and 8 patients in PGE2 group delivered within 12-24 hours.

In current study, 19 patients in PGE1 group and 22 patients in PGE2 group delivered vaginally in 24 hours. This was in accordance with the studies of Kumari et al.[13] The rate of caesarean section was more in PGE1 group compared to PGE2. Most common indication of LSCS in our study was failed induction, fetal distress and meconium stained amniotic fluid. There was no caesarean section performed for maternal indication. In our study, 2 patients (8%) in PGE1 and none in PGE2 group required LSCS due to failed induction. In a study by Calder et al, there was no significant difference between the two groups requiring LSCS due to failed induction.[12]

In this study, 4 patients (16%) in PGE1 group and 2 patients (8%) in PGE2 group complained of nausea, vomiting. 3 patients (12%) in PGE1 group and 1 patient (4%) in PGE2 group suffered from headache, statistically not significant. None of our patients from either group had uterine hyperstimulation, uterine tachysystole and uterine rupture. All the side effects were mild and well tolerated. None of the patient required any additional medication. In the study of Kumari et al, tachysystole and hyperstimulation was the major indications for LSCS.[13]

Neonatal outcome and perinatal results were evaluated by Apgar score and NICU admissions. In our study, 2 (8%) babies in prostaglandin E1 group, 1 (4%) baby in prostaglandin E2 gel group were admitted to neonatal intensive care unit, the difference is insignificant due to poor Apgar score. All the babies recovered well. There was no intrauterine fetal death or perinatal mortality. Gupta et al study had also reported similar perinatal outcome in both groups.[14]

CONCLUSION

In conclusion, both methods of induction (PGE1 and PGE2) were quite similar in safety and efficacy profiles barring few minor differences. However, as present study

has limited number of patients, and being a small-scale study, it would be advisable to conduct this study at a larger scale so that the similarities and differences can be precisely studied. Precise use of induction agents with careful selection of patients can be a useful method to reduce the perinatal morbidity and mortality. Prospective research is required to fully evaluate the impact of AMOR-IPAT on nulliparous birth outcomes.

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