

Premature rupture of membranes at term : immediate induction with PGE₂ gel compared with delayed induction with oxytocin

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OBJECTIVE(S) : To compare immediate induction with PGE₂ gel and delayed induction with intravenous oxytocin drip in women with premature rupture of membranes(PROM) at term.

METHOD(S) : In this prospective study 223 women were randomly assigned to either immediate induction with PGE₂ gel instilled in posterior fornix or expectant management for 12-24 hours followed by induction of labor with intravenous oxytocin drip. The two groups were compared with respect to mode of delivery, labor characteristics, and neonatal and maternal infectious morbidity.

RESULTS : Ninety-one percent of women required single application of PGE₂ gel for labor induction in immediate induction group. Thirty-two percent women had onset of spontaneous labor during observation in delayed induction group. Immediate induction with PGE₂ resulted in significantly lower rate of cesarean section (17.8% vs 28.5%, P = 0.049) and of lower rate of operative vaginal delivery (3.5% vs 14.2%, P=0.007) among nulliparous women. There was no significant difference in the mode of delivery among multiparas. Interval from induction to active labor, duration of active labor, and length of hospital stay before delivery were not significantly different between the two groups. The maternal morbidity was almost negligible. Only a few neonatal infections occurred and no significant difference was noted between the two groups (2.7% vs 3.5%, P= 0.71).

CONCLUSION(S) : In women with PROM at term, immediate induction of labor with PGE₂ gel and expectant management followed by oxytocin result in similar low rates of neonatal infection. Immediate induction of labor with PGE₂ gel results in significantly lower rate of cesarean section and of operative vaginal delivery in nulliparas.

Key words : premature rupture of membranes, induction of labor, induction with PGE₂ gel, oxytocin induction

Introduction

Premature rupture of membranes (PROM), which is defined as rupture of membranes before onset of labor, complicates 5-10 % of pregnancies. At least 60% of cases of PROM occur at term¹. In spite of many studies available in the literature, the clinical management is surprisingly controversial. The concern with conservative management is the risk of infection to the mother and the fetus whereas immediate induction can increase cesarean rate².

Both oxytocin and prostaglandin E₂ are effective in inducing labor in women with PROM at term¹. For labor that is induced, timing of induction is controversial³. Several studies have demonstrated the use of vaginal prostaglandin in women at term with PROM³⁻⁵. If induction is attempted with intravenous oxytocin drip in women with unfavourable cervix the possibility of failed induction and subsequent cesarean delivery approaches 30-40% and protracted labor increases the risks of maternal and neonatal infection¹. An expectant management followed by delayed induction with oxytocin will allow a good number of women to go into labor without an increase in cesarean section rate and infectious morbidity for mother and fetus^{2, 6,7}.

This study was undertaken to determine whether immediate induction of labor with PGE₂ gel is preferable to induction

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with intravenous oxytocin drip after an expectant management of 12-24 hours.

Methods

This prospective randomised controlled trial was conducted from January 2003 to June 2004. Women were eligible for entry into the trial if they had ruptured membranes at ≥ 37 weeks of gestation, had a single fetus in cephalic presentation and were not in labor. The time of spontaneous rupture of membranes was noted. Diagnosis was based on (i) clinical history of passage of liquor (ii) palpation through cervical canal (iii) pooling of fluid in posterior fornix as seen by speculum examination, and (iv) reduced liquor volume on sonography (AFI <5) in selected women where clinical findings were inconclusive. No other tests of spontaneous rupture of membranes, such as pH of the vagina or the presence of ferns on microscopy were made. At the time of diagnosis of rupture of membranes, Bishop scoring was also done, following which uterus was palpated by a medical staff for one hour and fetal heart sound was monitored. If the fetal heart rate was normal and if contractions were not palpated, women were randomly allotted to either immediate induction or delayed induction group. Randomization was done using a table of random numbers. Prophylactic antibiotic either of a penicillin group or a cephalosporin group, depending on the availability of the antibiotic in the hospital was given. Women were excluded from the study if they were in labor (onset of labor was defined as regular contractions occurring twice in 10 minutes detected by abdominal palpation) or if there was a contraindication to either induction of labor (such as placenta previa) or expectant management (such as meconium staining of amniotic fluid). Informed consent for inclusion in the study was requested by the medical staff and no woman refused it. A high vaginal swab was taken at the time of admission in 191 women.

In the immediate induction group labor was immediately induced by instillation of 0.5mg PGE₂ gel in the posterior fornix. Qualified medical staffs observed the woman closely. If labor had not supervened after 6 hours application of PGE₂ gel was repeated.

Women in the delayed induction group were closely observed by trained medical personnel for 12-24 hours. Monitoring included (i) temperature recording every 4 hours while awake (ii) fetal heart rate monitoring every hours while awake (iii) no digital vaginal examination until the woman was clinically in active labor, and (iv) induction if chorioamnionitis developed. The criteria for diagnosing chorioamnionitis were temperature more than 38°C with any two of the five features, viz. maternal tachycardia, fetal tachycardia, uterine tenderness, foul discharge and maternal leukocytosis. The woman was sent back to the

labor ward if fetal heart rate monitoring was nonreassuring or if she wanted to have analgesics due to uterine contractions of latent phase or she went into active labor.

If labor did not supervene in 12-24 hours since admission, induction of labor with an oxytocin infusion was done. Five units of oxytocin were placed in 500 mL of Ringer's solution and the infusion started at 2 mIU/minute. The oxytocin infusion rate was doubled every 15 minutes until three contractions were obtained in 10 minutes or until a maximum infusion rate of 32 mIU/minute was achieved. Vaginal examination was performed every 4 hours to assess the progress of labor. Abnormal labor was defined very specifically. Failure to progress in the latent phase was defined as a period of 24 hours in primigravidas and 14 hours in multigravidas without progress. Failure to progress in active phase of labor was defined as failure of further cervical dilatation after 3 cm dilatation or of descent of the presenting part after 2 hours of adequate uterine contractions. Failure to progress in the second stage of labor was defined as the absence of further descent of presenting part over a period of 2 hours in primigravidas and 1 hour in multigravidas in spite of adequate uterine activity.

At delivery apgar scores were determined. Babies in both the groups had a blood sample taken for white cell counts and culture within 24 hours of birth and before treatment with antibiotics. Other tests and treatment given to the babies were determined by attending pediatricians. Statistical analysis was performed using Epi Info program and Z test and chi square test were used to determine test of significance.

Results

Of the 223 women 111 were assigned to the immediate induction (PGE₂ gel) group and 112 to the delayed induction (expectant management followed by oxytocin) group. Baseline characteristics were similar in both the groups (Table 1).

Methods of induction of labor and use of oxytocin during labor are shown in Table 2. In delayed induction group 32.14 % (36/112) women went into spontaneous labor while under observation. The modes of delivery according to parity in the immediate induction and delayed induction groups are shown in Table 3. The rate of cesarean section among nulliparous women was higher in delayed induction group but only marginally significantly so (28.5% vs 17.8%, $P=0.049$). Operative vaginal delivery rate was significantly higher in delayed induction group (14.2% vs 3.5%, $P=0.007$). In the immediate induction group 12 cesarean sections had to be carried out for labor dystocia

Table 1. Baseline characteristics of women in immediate and delayed induction groups.

| Characteristic | Immediate induction (n=111) | Delayed induction (n=112) | P value |
|---|--------------------------------|------------------------------|---------|
| Maternal age (years) ^a | 23.2 ± 3.9 | 23.9 ± 4.7 | 0.02 |
| Gestational age (weeks) ^a | 38.7 ± 1.3 | 38.0 ± 1.1 | 0.01 |
| Parity 0 | 84 (75.67%) | 85 (75.0%) | |
| ≥ 1 | 27 (24.32%) | 28 (25.0 %) | |
| Ultrasound needed to confirm gestational age | 102 (91.89%) | 84 (75.0%) | 0.0006 |
| Interval from rupture of membranes to admission (hours) | | | |
| Methods of confirming rupture of membranes | | | |
| Pooling of amniotic fluid on speculum examination | 87 (72.97%) | 96 (85.71%) | 0.153 |
| Absence of membranes on digital examination | 81 (72.97%) | 92 (82.14%) | 0.100 |
| Reduced liquor volume on USG (AFI < 5) | 6 (5.40%) | 4 (3.57%) | 0.508 |
| Bishops score ≥ 6 | 36 (32.43%) | 34 (30.35%) | 0.738 |
| < 6 | 76 (67.56%) | 78 (69.64%) | 0.738 |
| Presence of group B streptococci in vaginal culture | 9 (8.0%) | 11 (9.8%) | 0.654 |

^a values are Mean ± S.D.

Table 2. Methods of inducing labor and use of oxytocin during labor in immediate and delayed induction groups.

| | Immediate induction (n=111) | Delayed induction (n=112) |
|------------------------------|--------------------------------|------------------------------|
| PGE ₂ only | 102 (91.89%) | -- |
| Oxytocin only | -- | 76 (67.85%) |
| Repeat PGE ₂ | 9 (8.10%) | -- |
| Not induced | 0 | 36 (32.14%) |
| Use of oxytocin during labor | 36 (32.43%) | 92 (82.14%) |

Table 3. Modes of delivery in immediate and delayed induction groups.

| | Immediate induction (n=111) | Delayed induction (n=112) | Z value | P value |
|------------------------------|--------------------------------|------------------------------|---------|---------|
| Parity 0 | | | | |
| Cesarean section | 15 (17.8%) | 24 (28.5%) | 1.646 | 0.049 |
| Operative vaginal delivery | 3 (3.5%) | 12 (14.2%) | 2.437 | 0.007 |
| Spontaneous vaginal delivery | 66 (78.5%) | 48 (57.14%) | 2.962 | 0.001 |
| Total | 84 (100%) | 84 (100%) | | |
| Parity ≥ 1 | | | | |
| Cesrean section | 0 | 0 | | |
| Operative vaginal delivery | 2 (9.4%) | 0 | | |
| Spontaneous vaginal delivery | 25 (92.5%) | 28 (100%) | 1.498 | |
| Total | 27 (100%) | 28 (100%) | | |

Table 4. Maternal outcome in the immediate and delayed induction groups.

| Outcome measure | Immediate induction (n=111) | Delayed induction (n=112) | P value |
|---|--------------------------------|------------------------------|---------|
| Clinical chorioamnionitis | 0 | 0 | |
| Analgesic use | 66 (59.4%) | 64 (57.1%) | 0.725 |
| Fetal distress | 3 (2.7%) | 4 (3.5%) | 0.71 |
| Antibiotics before or during labor | | | |
| Penicillin | 78 (59.4%) | 68 (53.5%) | 0.13 |
| Cephalosporin | 33 (29.7%) | 4 (43.9%) | 0.133 |
| Number of vaginal digital examinations | | | |
| < 4 | 66 (59.4%) | 60 (53.5%) | 0.375 |
| 4 to 8 | 45 (40.5%) | 52 (46.4%) | 0.375 |
| Time taken from induction to 3 cm dilatation (hours) ^a | 4.7 ± 4.2 | 5.73 ± 4.2 | 0.067 |
| Duration of active labor (hours) ^a | 3.89 ± 2.6 | 3.79 ± 2.0 | 0.749 |
| Interval from rupture of membranes to delivery (hours) ^a | 17.10 ± 10.3 | 21.63 ± 10.3 | 0.001 |
| Postpartum fever | 2 (1.8%) | 1 (0.8%) | 0.55 |
| Hospital stay before delivery (hours) ^a | 16.03 ± 8.6 | 17.52 ± 9.2 | 0.21 |

^a Values are Mean ± <SD.

Table 5. Neonatal outcome in the immediate induction and delayed induction groups.

| Outcome measure | Immediate Induction (n=111) | Delayed Induction (n=112) | P Value |
|---|--------------------------------|------------------------------|---------|
| Apgar score < 7 at 1 min. | 6 (5.4%) | 8 (7.1%) | 0.59 |
| < 7 at 5 min. | 0 | 0 | |
| Resuscitation with oxygen | 6 (5.4%) | 5 (4.4%) | 0.74 |
| Ventilation after initial resuscitation | 0 | 4 (3.5%) | |
| Stay in intensive neonatal care unit | 3 (2.7%) | 4 (3.5%) | 0.71 |
| Feeding problems at 48 hours of age | 3 (2.7%) | 4 (3.5%) | 0.71 |
| Neonatal infection | 3 (2.7%) | 4 (3.5%) | 0.71 |

and three for fetal distress. In the delayed induction group 20 cesarean sections had to be carried out for labor dystocia and four for fetal distress. There was no difference in the mode of delivery in the two groups among multiparas.

We also examined the rate of cesarean section in the two groups considering Bishops score at the time of randomizing to study groups. At randomization, in the immediate induction group 75 women had a Bishop score

< 6 and in them the rate of cesarean section was 20% (15/75). In the delayed induction group 74 women had a Bishop score < 6 and the rate of cesarean section was 27.02% (20/74). Maternal outcome in regard to clinical chorioamnionitis, analgesic use, number of digital vaginal examinations during labor, interval from induction to delivery, postpartum fever, and hospital stay before delivery were similar in both the groups (Table 4). Blood samples were taken for white cell count and culture in more than 70% of babies in the two groups. The rate of

neonatal infection did not differ significantly between immediate and delayed induction group (2.7 % vs 3.57 %; P=0.71) (Table-5).

Discussion

PROM is not uncommon yet the management, even at term, is controversial and there is no standard protocol for management.

Among the 223 women who were included in the study, 168 (75.33%) were nulliparas. Kodkany and Telang ⁸ and Semezuek–Sikora et al ⁹ also had greater number of primigravidas.

In the immediate induction group 91.89 % (102/111) women required only a single application of PGE₂ gel for induction. This is similar to the observation of Gonen et al ¹⁰ who report that 93 % of women began labor after a single application of PGE₂ gel. Ben-Haroush et al ¹¹ report 80% success rate with induction by vaginal insertion of PGE₂ tablets.

In the delayed induction group 32.14% women had spontaneous onset of labor while under observation. This is similar to the observation of George et al ² that 35.6% of primigravidas went into spontaneous labor within 12 hours.

The rate of cesarean section among nulliparas in immediate induction group was 17.8%. Similar cesarean section rate was observed by Ben-Haroush et al ¹¹ and Lettau et al ¹². There are many studies that have demonstrated a lower cesarean section rate by expectant management for variable period ^{7,13,14}. In a large randomized prospective trial of over 5000 women, Hannah et al ⁴ found no difference in the rate of cesarean section among immediate induction and conservative management groups. In our study the rate of cesarean section in delayed induction group was higher (28.5% vs 17.8%, P=0.049) among nullipara. Similar high cesarean section rate was observed with delayed induction with oxytocin in other studies ^{7,14,15}. A similar cesarean section rate with PGE₂ was observed by Choudhuri and Naheed ⁵ and Carbonne et al ³ when compared with expectant management followed by oxytocin. Operative vaginal delivery (forceps or ventouse) was significantly higher in delayed induction group nulliparas (14.2% vs 3.5% , P=0.007). Perhaps this reflects inefficient uterine action or possibly indicated that our management of these women was not aggressive enough. Conway et al ⁷ also made similar observation.

Many studies have demonstrated shorter induction to delivery interval, shorter duration of active labor, decreased number of vaginal examinations, and decreased analgesic use with immediate induction, when compared with expectant

management or delayed induction ^{2,4,5,15}. In our study no such advantage with immediate induction was noticed when compared to delayed induction. This might be due to the fact that in our study we have observed the women for only 12-24 hours and 32.14% of women had spontaneous onset of labor during observation thereby influencing the overall outcome. However interval from rupture of membranes to delivery was significantly shorter in immediate induction group (P=0.001).

Hannah et al ⁴ in their randomized controlled trial had concluded that immediate induction with intravenous oxytocin and conservative management result in similar rates of neonatal infection but immediate induction results in lower risk of maternal infection. In their study they observed the patients upto four days but in our study we observed the patients only for 12-24 hours. In our study maternal and neonatal infection rate in both the groups were low. Similar low rates of maternal and neonatal infection in immediate and delayed induction groups were observed in other studies also ^{6,7}.

Conclusion

In nulliparous women immediate induction with PGE₂ gel results in lower cesarean section rate when compared with delayed induction. In parous women both PGE₂ and oxytocin are effective and safe. Infective morbidity of mother and baby was low and no difference was observed in immediate and delayed induction group.

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