https://doi.org/10.22502/jlmc.v2i1.46

Original Research Article

Induction of Labour in Prelabour Rupture of Membranes with or without Cervical Ripening with Prostaglandin E2: A Randomized Controlled Trial

Shreyashi Aryal[a], Chanda Karki[b].

ABSTRACT:

Objective: To compare the outcome of induction of labour with titrated dose of oxytocin with or without pre induction cervical ripening using prostaglandin E2. **Methods**: This is a prospective study. Sixty women with prelabour rupture of membranes (PROM) and Bishops score of less than six were randomly assigned to either immediate induction with intravenous oxytocin drip or induction with intravenous oxytocin drip preceded by cervical priming with prostaglandin E2 (PGE2) gel 0.5mg instilled intracervically. These two groups were compared regarding the mode of delivery, induction to delivery interval and maternal and neonatal morbidities. **Results**: Cervical priming with PGE2 resulted in lesser number of caesarean section (5 Vs. 12) and lower incidence of meconium stained liquor (*n*=6 Vs. *n*=2). Induction to vaginal delivery interval was shorter when cervical priming was done (5.4 hrs Vs 7.9 hrs). The maternal morbidity was negligible (<1%) in both the groups. The number of neonates with birth asphyxia (*n*=2) and the need for their resuscitation (*n*=2) was more in the oxytocin group but the need of antibiotics for the neonates was more in PGE2 group (5% Vs. 3%). **Conclusion**: Induction of labor with oxytocin, with or without cervical priming with vaginal PGE2 gel, are both reasonable options in cases of PROM, since they result in statistically non significant rates of maternal and neonatal morbidities and caesarean section. Cervical priming with prostaglandin results in higher rate of vaginal delivery and shorter induction to vaginal delivery interval and this is viewed as an advantage to the mother.

Keywords: induced labor • premature rupture • oxytocin • prostaglandin • cervical ripening

INTRODUCTION:

Rupture of membranes before the onset of labour is termed as prelabour rupture of membranes (PROM) and the incidence is reported to be 8% to 10% of all pregnancy.[1-3] It is also defined now as rupture of membranes at least one hour prior to the onset of labor.[4] Prolonged PROM is defined as an interval greater than 24 hours between PROM and active phase of labour.[5]

Fetal membranes serve as a barrier to ascending infection so once rupture of membranes occur, there is increased risk of infection, both to the mother and the fetus.[6] PROM is associated with significant maternal risks mainly chorioamnionitis and the postnatal risks include endometritis and pelvic infection.[7] Intrapartum risk factor relate to obstetric interventions mainly induction, which when done with unfavorable cervix often leads to prolonged labour and higher risk of operative delivery. The main fetal problem is also related to infection along with risk of fetal hypoxia as a consequence of cord compression, cord prolapse and placental abruption.[6]

The management of PROM lies somewhere in between expectant management up to 48 hours or immediate induction of labour. The exact management will have to take into consideration, parental wishes, parity, cervical favorability and signs of chorioamnionitis but the best solution is

a - Lecturer, Department of Obstetrics and Gynaecology, Lumbini Medical College Teaching Hospital, Palpa, Nepal

b - Professor, Department of Obstetrics and Gynaecology, Kathmandu Medical College Teaching Hospital, Sinamangal, Kathmandu, Nepal

Corresponding Author:
Dr. Shreyashi Aryal
e-mail: shreyashiaryal@gmail.com

How to cite this article:
Aryal S, Karki C. Induction of Labour in Prelabour Rupture of Membranes with or without Cervical Ripening with Prostaglandin E2: a randomized controlled trial. Journal of Lumbini Medical College. 2014;2(1):4-9. doi: 10.22502/jlmc.v2i1.46.

delivery. Most patients of PROM will go into labour spontaneously so that, in the absence of intervention, only about 2-5% remains undelivered after 48 hours.[8] Induction is done in the remaining cases to prevent various maternal and neonatal complications.

This study is done to compare the maternal and neonatal outcome in two different management schemes of induction in cases of PROM.

METHODS:

This is a hospital based randomized, interventional, prospective study conducted at the Department of Obstetrics and Gynaecology, Kathmandu Medical College Teaching Hospital, Sinamangal for the time period of one year, November 1st 2011 to October 31st 2012. The study was approved by the ethical committee of the hospital.

During this time period, the total number of nulliparous ladies presenting with PROM was identified. These nulliparous ladies included primigravidas as well as virtual primigravidas i.e, the patient in her second pregnancy, the first having ended in an abortion. The main inclusion criteria were nulliparous women with singleton, term pregnancy (37-42 weeks of gestation) with cephalic presentation with diagnosed PROM. High vaginal swab was taken and sent for culture and sensitivity and all diagnosed cases were given prophylactic antibiotics as per the hospital protocol. The exclusion criteria were Bishops score more than or equal to six, previous uterine scar, chorioamnionitis, antepartum hemorrhage, cephalopelvic disproportion, meconium stained amniotic fluid, severe oligohydramnios (AFI of 4 centimeters or less), severe pre eclampsia, history of allergy to prostaglandins and those unwilling to participate.

After taking informed consent, the identified cases were then allocated randomly to one of the two groups with the help of computer generated random numbers. The two groups were managed as follows.

Group A: Induction of labour was done with intravenous oxytocin in titrating dose infused at the rate of 6.25 mIU/min (10 drops/min) and gradually increasing the dose every 30 minutes in case of inadequate contractions, to a maximum dose of 37.5mIU/min (60 drops/min). Adequate contractions were taken as 3 contractions in 10 minutes each lasting for more than 40 seconds.

Group B: Induction of labour was done with titrating doses of oxytocin following cervical ripening with PGE2 gel. Cervical ripening was done by 0.5mg PGE2 gel (Dinoprostone gel) inserted intracervically every six hours upto three doses until the Bishops score was six or more. Cervix was assessed every six hourly to find out the improvement in Bishops score. In the process of cervical assessment when the Bishops score was found to be more than or equal to six, induction with oxytocin was immediately started but in this process if before the scheduled time of cervical assessment, adequate uterine contractions were noted, per vaginal examination was done before the scheduled time for cervical assessment. If at this time, Bishops score was more than or equal to six, further cervical priming was not done but induction was done with oxytocin after six hours from the last dose of PGE2. Oxytocin was then infused in the same way as in group A to maintain the adequate contractions.

Those patients who developed adequate contractions and delivered with cervical priming with PGE2 without the use of oxytocin were noted separately. A group of clients who neither showed improvement in Bishop's scoring nor progressed into adequate uterine contractions with three doses of dinoprostone gel were also managed with oxytocin infusion with titration. Failed induction was considered if the subject did not go into active phase of labour after twelve hours of induction with oxytocin.

According to the hospital protocol, babies with PROM for more than 18 hours were admitted for observation in the NICU for presumed sepsis. Antibiotics were given to those neonates who were diagnosed to have probable or confirmed sepsis. A neonate suspected clinically to have sepsis, with C-reactive protein positive and at least one of the following rapid diagnostic tests positive- absolute neutrophil count, thrombocytopenia, toxic granules in the peripheral smear, or a band count of greater than 500/mm³ was said to have probable sepsis. The blood culture was negative. When the blood, urine or cerebrospinal fluid culture yielded an organism, then the neonate was diagnosed as confirmed sepsis and antibiotics were started. The neonates admitted in the neonatal intensive care unit were followed up till discharge. The neonates with presumed sepsis were discharged from NICU if the blood or urine culture and sensitivity reports showed no growth. Neonates with other complications were discharged as per the NICU protocols.

The reports of high vaginal swab culture and sensitivity were collected from the laboratory and treatment given if required, before discharging the patient. All the clients were followed up daily till one week postpartum. After discharge they were contacted through telephone on the seventh postoperative day.

All relevant data for each individual study subjects were collected and recorded in a predesigned data collection sheet. All data were analyzed using

Statistical Package for Social Sciences (SPSS) version 11. Pearson's or Fisher Exact test, Chi square test were used and *p* value was calculated. $p < 0.05$ was considered to be statistically significant.

RESULTS:

During the study period of one year, there were total 2606 antenatal obstetric admissions in this department. The incidence of PROM among all antenatal admissions during this period was 5.7 %. There were 149 cases of PROM who were admitted out of which, 89 cases did not meet the inclusion criteria and therefore were excluded from the study. The cases that were excluded were multigravida (36), Bishops score <6 (20), cephalopelvic disproportion (11), no evident leaking (8), meconium (4), severe oligohydramnios (4), fetal heart rate abnormalities (2), breech (2), twin (1), severe pregnancy induced hypertension (1).

Sixty primigravida ladies meeting the inclusion criteria were randomized into each of group A and B. Table 1 shows the demographic characteristics of both the groups. Table 2 shows the antenatal parameters which are comparable. Regarding the duration of gestation, 76% of the clients were between 37 to 40 weeks of gestation and no clients were post term.

Table 1: Demographic Distribution

	Group A	Group B	*p*
Age, *SD*	24.13, 3.93	23.70, 3.08	0.205
Parity (n)			
Primigravida	27	26	0.201
Virtually Primigravida	3	4	
BMI(kg/m²)	27. 03	27.25	0.208
Education status			
Illiterate	0	0	
Primary	3	5	
Secondary	8	6	
Higher Secondary	12	8	
Bachelors	6	4	
Masters	1	7	

The interval between PROM and delivery is known as the latent period and neonatal morbidities are increased when latent period is more than 18 hours. The results of this study show seven cases (four in group A and three cases in group B) with prolonged PROM.

Table 2: Distribution of cases according to antenatal parameters

	Group A	Group B	*p*
Adequate Antenatal check up (>4), *n* **(%)**	30 (100%)	29 (96.6%)	0.205
Gestational age(wks) *M,SD*	39.35, 1.13	38.89, 1.16	0.201
Preinduction Bishop score	4.3	4.3	
Antenatal risk factors			
Young primi (<19yrs)	3	0	
Rh negative pregnancy	1	1	
Obstetric cholestasis	1	0	
Mild Pregnancy induced hypertension	1	1	
Duration of PROM (hrs)			
1-6	16	10	
7-12	4	11	
13-18	6	6	
>19	4	3	
High risk factors for PROM noted in the study			
UTI	3	6	
Anemia (Hb < 11gm%)	2	6	
Low socioeconomic status	7	2	
Elderly primigravida (Age >34yrs)	0	1	
Smoking	0	0	

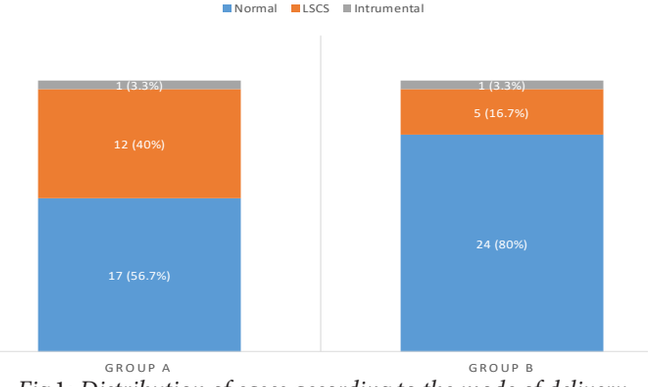

Fig 1: Distribution of cases according to the mode of delivery

Fig. 1 shows the mode of delivery in the two groups and Table 3 shows the delivery details of both the groups. When cervical priming was done with prostaglandins, vaginal delivery rate is shown to be higher (80%) and the induction to vaginal delivery interval is also found to be shorter.

The total number of vaginal examinations done was also noted since more number of vaginal examinations are related to higher rates of maternal

Table 3: Distribution of cases according to delivery details

Variables	Group A	Group B	*p*
Vaginal delivery, *n*	17	24	0.369
LSCS, *n*	12	5	
Indication for LSCS			
Fetal Distress			
fetal heart rate abnormalities: *n*(%)	4(33.33)	2 (40)	
meconium stained liquor: *n*(%)	3 (25)	0	
Failed induction	4 (33.33)	0	
Outlet CPD: *n*(%)	1 (8.33)	1 (20)	
Instrumental delivery:			
Vacuum delivery, *n*(%)	1(3.33%)	1(3.33%)	
Forceps delivery, *n*(%)	0	0	
Average no. of vaginal examinations (*n*)	3.4	4.1	
Induction to delivery time in hrs (*M, SD*)	7.13, 3.84	7.23, 3.68	0.512
Induction to caesarean delivery time in hrs (*M,SD*)	6.23, 2.74	8.23, 3.51	0.126
Induction to vaginal delivery interval in hrs (*M, SD*)	7.95, 3.53	5.42, 2.83	0.254
Meconium stained amniotic fluid (*n*)	6	2	0.428

Table 5: Distribution according to the neonatal outcome

	Group A	Group B	*p*
Apgar score, 1' (*M,SD*)	6.9, 1.74	7.4, 0.66	0.463
Apgar score, 5' (*M,SD*)	7.9, 1.7	8.4, 0.49	0.521
Need of resuscitation (*n*)			
Bag and Mask	1	0	
Mechanical ventilation	1	0	
Sex			
Male	18	17	0.13
Female	20	13	
Birth Weight Kg (*M,SD*)	2.93, 0.31	2.94, 0.30	0.177
<2.5kg	1	4	
2.5-4kg	29	26	
Neonatal jaundice (*n*)	1	0	
Perinatal death (*n*)	1	0	
Admission to neonatal unit (*n*)	16	12	
Indication for neonatal admission:			
Presumed Sepsis	120	10	
Birth asphyxia	2	0	
Congenital Anomaly	1	1	
Jaundice	1	0	
Rh negative mother	0	1	
Need of antibiotics (*n*)	3	5	0.212

and neonatal infection. The number of vaginal examinations was higher in group B as multiple doses of prostaglandins were used in this group.

The maternal complications were negligible in both the groups (Table 4). One client in group B had wound infection following lower segment caesarean section for fetal distress which required a secondary suturing. The vaginal swab which was sent for culture and sensitivity in an aerobic media showed no growth for all 60 clients. Absence of growth could be due to the use of a non selective media used in the laboratory.

Table 4: Distribution of cases according to maternal morbidities

Maternal complications	Group A	Group B
Nausea	0	1
Vomiting (>2episodes)	1	1
Diarrhoea	0	0
Fever	0	0
Hyperstimulation	0	0
Chorioamnionitis	0	0
Perineal tear (Episiotomy excluded)		
first degree	2	2
second degree	1	1
third and fourth degree	0	0
Postpartum haemorrhage	0	0
Puerperal pyrexia	0	0
Wound infection (requiring secondary suturing)		
Episiotomy wound	0	0
LSCS wound	0	1
Hospital stay in days (*M,SD*)	2.7, 1.4	2.4, 2.2

The neonatal outcome was similar in both the groups in terms of birth weight and sex (Table 5). A good Apgar score and the need of resuscitation are some of the indicators for a good neonatal outcome. The need of resuscitation besides tactile stimulation was recorded in this study and 3.3% babies needed resuscitation of some form besides tactile stimulation. The need of resuscitation was more in group A. The most common indication for admission was presumed sepsis in both the groups.

DISCUSSION:

PROM is one of the common and challenging problems in perinatal medicine and its management has gone through various cycles from inactivity and expectant management to immediate intervention.

Incidence of PROM in the present study

is 5.7% among all antenatal admissions which is similar to other studies done within the country,[9-11] but is lower than the incidence of 8-10% shown in different studies in the United States.[2,3] One of the main objectives of this study was to compare the mode of delivery between the two groups. In these two groups with similar demographic characters, it was observed that the number of vaginal delivery was more in the group where prostaglandin was used. Induction following good cervical ripening seems to reduce caesarean section which is also shown by Gungorduk et al. where a single dose of sustained release dinoprostone pessary was used before oxytocin infusion and by Chaudhury S. et al. where vaginal delivery rate was higher when prostaglandin was used.[12,13]

In a study by Chiong TP. where concurrent prostaglandin pessary and oxytocin was used, the rate of fetal distress was more and thus vaginal delivery rate was only 59.6% which is significantly lower than this study.[14]

The results of this study show the use of prostaglandins for cervical ripening has reduced the rate of LSCS for failed induction, compared to induction without cervical priming which highlights its importance.

Also, unfavorable Bishop score at admission for induction of labour are associated with a two to three fold increased risk of caesarean delivery, whereas a score of six or more is usually associated with a probability of vaginal delivery after labour induction, similar to that after spontaneous labour.[15,16] In this study the use of dinoprostone gel for induction of labour, improved the Bishop score so chances of successful induction also increased.

In the analysis of the presence of meconium stained amniotic fluid after cervical priming, use of prostaglandin reduced the induction to delivery interval and decreased chances of fetal hypoxia. More the latent period in PROM, more are the chances of poor maternal and fetal outcome.[7] This stresses the importance of cervical priming to shorten the induction to delivery interval in cases of PROM. Gungorduk et al. and Chiong TP. showed a longer induction to delivery interval compared to this study in both the groups.[12,14]

Regarding the maternal morbidities in the two groups, though the induction to delivery interval was short in cases where prostaglandin was used, there was no clear advantage to the mother in terms of intrapartum and postpartum morbidities. Various studies have shown the incidence of tachysytole with the use of prostaglandins.[12,14] Since this study has no cases of uterine hyperstimulation or tachysystole, it is suggestive that PGE2 use for cervical priming is a safe option in cases of PROM. With no adverse effects and the benefits of ability to be mobile and not attached to an intravenous infusion makes the use of PGE2 for cervical ripening in cases of PROM more desirable.

One of the likely complications of PROM is chorioamnionitis. In an evaluative study derived from international multicentre Term Prelabor Rupture of Membranes Study, incidence of chorioamnionitis was 7% and postpartum fever was 3% whereas in our study, there were no cases of either postpartum fever or chorioamnionitis.[17] This difference could be due to the large difference in sample size in the two studies and probably due to early induction and the use of prophylactic antibiotics at the time of diagnosis.

The mean induction to delivery interval of seven hours in both the groups suggests that the delivery of the baby was within 24 hours after PROM which carries a better prognosis for the neonate. There were fewer admissions to neonatal care ward in the group where prostaglandins was used but there were more number of neonates who required antibiotics in this group. This is probably due to the increased number of vaginal examinations done for prostaglandin insertion and increased chances of sepsis. In a study by Hellen YM. et al., two neonates were diagnosed with infection when prostaglandin was used, whereas no cases of infection was seen in the oxytocin group which is similar to this study where more neonates were tested positive on septic screening in Group B.[18]

In this study, all ladies with PROM were given oral Amoxycillin capsules as per the department protocol whereas in the previous mentioned studies antibiotics given to the subjects is not mentioned so this could be the reason for variation seen in neonatal infection rate but the study by Shrestha SR. et al. shows no difference in neonatal infection rate after the mother received IV penicillin.[10-12,18]

Traditionally, oxytocin induction has been recommended for the induction of labour in the management of PROM with an unfavorable cervix. The results of this study show that cervical priming which improves Bishops score, results in a higher number of vaginal delivery and results in a decreased caesarean section rate especially for the indication

of failed induction.

The recommendations from this study with a relatively small sample size may not be sufficient to come to a conclusion for all the parameters measured in this study and further larger trials would be required, probably with a third arm undergoing expectant management.

CONCLUSION:

In cases of PROM, if timely diagnosis and administration of prophylactic antibiotics is done, the results of labour induction with or without cervical priming are comparable. Cervical priming with PGE2 results in a higher rate of vaginal delivery and shorter induction to vaginal delivery interval. Therefore, in terms of mode of delivery, cervical priming is recommended when the cervix is unfavourable. Since no drug related complications were observed, cervical priming is a considerable option keeping in mind the lower number of caesarean sections following cervical ripening. In view of neonatal morbidities and NICU admissions, both the options of induction with or without cervical priming seem to be acceptable. We can conclude that induction of labour with intravenous oxytocin, with or without cervical priming with vaginal prostaglandin E2 gel, are both reasonable options for women and their neonates in cases of PROM, since they result in similar rates of intrapartum and postpartum maternal morbidities and neonatal morbidities.

REFERENCES:

1. Robinson JS. Prelabour rupture of membranes. In: James DK, Steer PJ, Weiner CP, Gonik B, editors. High Risk Pregnancy Management Options, 3rd ed., India: Elsevier; 2006.p.1321-28.
2. American College of Obstetricians and Gynecologists Committee on Practice Bulletins—Obstetrics. Premature rupture of membranes: Clinical management guidelines for obstetrician-gynecologists. ACOG Practice Bulletin No. 80. Obstet Gynecol. 2007;109(4):1007–19.
3. Poma PA. Premature rupture of membranes. J Natl Med Assoc. 1996 Jan;88(1):27-32.
4. Sullivan R. Prelabour rupture of membranes at term. In: Bonnar J, Dunlop W, editors. Recent advances in Obstetrics and Gynaecology 23, London: Royal society of medicine press; 2005.p. 27-37.
5. Kui Li, Yanping W, Haiyan Li, Huixia Y. A study of 579 pregnant women with premature rupture of membranes at term. International Journal of Gynecology and Obstetrics. 2011;112:45–7.
6. D' Souza AS. Prelabour rupture of membranes. In: Arulkumaran S, Penna LK, Roa KB, editors. The Management of Labour, 2nd ed., Chennai: Orient Longman; 2005.p.306-18.
7. Induction of labour. In: Cunningham FG, Leveno KJ, Bloom SL, Hauth CJ, Rouse DJ, Spong CY, editors. Williams Obstetrics, 23rd ed., USA: McGraw Hill; 2010.p.500-9.
8. Prelabour rupture of membranes. In: Majhi AK, editor. Bedside Clinics in Obstetrics, Kokatta: Academic publishers; 2011.p.6.2.1-2.2.
9. Gautam J. Fetal outcome of premature rupture of membranes [thesis]. Kathmandu: T.U.; 1997.
10. Shrestha SR, Sharma P. Fetal outcome of pre-labor rupture of membranes. N. J. Obstet. Gynaecol. 2006 Nov-Dec;1(2):19-24.
11. Reproductive health clinical protocol for medical officers. Family Health Division, Dept. of health services, Ministry of Health and Population. Government of Nepal. 2007, 52-56
12. Gungorduk K, Asicioglu O, Besimoglu B, Gungorduk OC, Yildirm G, Ark C, et al. Labor induction in term premature rupture of membranes: comparison between oxytocin and dinoprostone followed 6 hours later by oxytocin. Am J Obstet Gynecol. 2012 Jan;206(1):60-68.
13. Chaudhuri S, Mitra SN, Biswas PK. Premature rupture of membranes at term: immediate induction with PGE2 gel compared with delayed induction with oxytocin. J Obstet Gynecol India. 2006 May/Jun;56(3):224-29.
14. Chiong TP. Concurrent Dinoprostone and Oxytocin for Labor Induction in Term Premature Rupture of Membranes. Obstet Gynaecol. 2009;113(5):1059-65.
15. Qualls CR, Rappaport VJ, Rayburn WF. Randomized trial of concurrent oxytocin with a sustained- release dinoprostone vaginal insert for labor induction at term. Am J Obstet Gynecol. 2002;186:61-5.
16. Tan PC, Valiapan SD, Tay PY, Omar SZ. Concurrent oxytocin with dinoprostone pessary versus dinoprostone pessary in labor induction of nulliparas with an unfavorable cervix: a randomized placebo-controlled trial. BJOG. 2007;114:824-32.
17. Seaward PG, Hannah ME, Myhr TL, Farine D, Ohlsson A, Wang EE, et al. International multicenter Term PROM study: Evaluation of predictors of neonatal infection in infants born to patients with premature rupture of membranes at term. Am J Obstet Gynecol.1998;179(3):635-9.
18. Helen YM, Andrew CB, O'Brien S. A comparison of oral prostaglandin E2 tablets with intravenous Oxytocin for stimulation of labor after premature rupture of membranes at term. Acta Obstetricia et Gynecologica Scandinavica. 1988;67(8):703-9.