A randomized study comparing intravaginal Prostaglandin (PGE2) with oxytocin for induction of labour in premature rupture of membrane at term

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ABSTRACT

This is a prospective randomized study conducted in Tribhuvan University Teaching Hospital from February 2008 to January 2009. Total 72 women with Premature rupture of membranes (PROM) were included. Thirty-six women received PGE_2 vaginal gel and thirty-six received iv oxytocin. Induction was successful in majority of cases in both the groups; 88.8% in PGE_2 and 83.3% in oxytocin group (p value = 0.063). Time duration from induction to active stage was comparable (p value = 0.273). Induction to delivery interval was significantly low in oxytocin group (p value = 0.002) but leaking to delivery interval was similar in both the groups (p value = 0.083). PGE_2 had slightly higher side effect than oxytocin. PGE_2 and oxytocin were both effective and safe for induction of labour in women with PROM at term. There was no significant difference in maternal and fetal outcome, hospital stay, leaking to delivery interval, maternal and neonatal side effects, though induction to delivery interval was significantly less with oxytocin.

Keywords: Induction, labour, oxytocin, premature rupture of membrane, prostaglandins.

INTRODUCTION

Labour is the onset of painful regular uterine contractions with progressive cervical effacement and dilatation accompanied by descent of presenting part resulting in expulsion of fetus from the uterus.[1] Premature rupture of membranes (PROM) is defined as rupture of membranes before the onset of labour. PROM occurs in 8-10% of all pregnancies and in 80% of the cases it occurs at term.[2,3] Labour usually starts spontaneously within 24 hours following term PROM, and upto 4% will not experience spontaneous onset of labour within seven days.[4]

With expectant management approximately 60- 80% of women with term PROM go into labour within 24 hours and 95% within 72 hours.[5] If the interval from leaking to delivery exceeds 18 hours there is an increase in incidence of neonatal infections and admissions. Induction of labour is the only strategy besides expectant management of term PROM that reduces the infectious morbidity for both mother and infant. Various agents have been introduced to stimulate uterine contractions and for cervical ripening but only few have been scientifically evaluated. Intravenous Oxytocin and different preparations of prostaglandins have been used for inducing labour but the effectiveness of all these agents varies.

There are very few prospective studies to assess the efficacy of prostaglandin E_2 vaginal gel in posterior fornix for labour induction in pregnant women at term PROM with poor Bishop Score. This study was done to evaluate the effectiveness and safety of vaginal Prostaglandins E_2 in induction of labour in women with term PROM with low Bishop Score.

MATERIALS AND METHODS

This is a prospective randomized study conducted between February 2008 to January 2009. All the pregnant women presenting to the labour room and who met the following criteria were included in the study: pregnancy at $\geq$ 37 weeks of gestation, parity less than 3, singleton pregnancy with vertex presentation, spontaneous rupture of membrane of <12 hours , no evidence of labour, Bishop Score $\leq$ 6, reassuring cardiotocography (CTG). Diagnosis of PROM was made if any of the following findings were present: sterile speculum examination revealed pooling of amniotic fluid in the posterior fornix, amniotic fluid coming out through the cervical os or introitus on coughing, or without coughing, pad soaked in the 2 hours of observational period if no liquor seen during examination, membrane absent in a woman with history of leaking per vaginum.

Two envelopes labeled as A and B were made. Envelop labeled A represented receiving PGE_2 and B represented receiving oxytocin. The first woman picked up envelop A, she received PGE_2 and following all the odd number received PGE_2 while the subsequent women having even number received oxytocin. Group A (Prostaglandin E_2 group): 1 mg of Prostaglandin E_2 was kept in posterior fornix and women were kept in

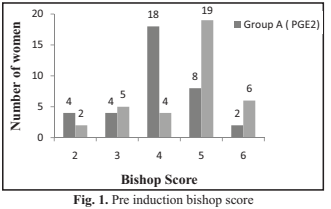

Fig. 1. Pre induction bishop score

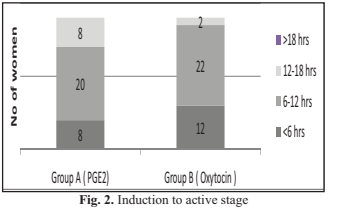

Fig. 2. Induction to active stage

left lateral position for half an hour. If uterine activity didn't start and Bishop score remained same, same dose was repeated after 6 hours. Group B (Oxytocin group): Dose of oxytocin used was 5 units for primigravidae and 2.5 units for multigravidae in titrating dose starting from 10 drops/min, accelerating at the rate of 10 drops/min every half an hour (max . 60drops/min). Maxmium of three pints of iv fluid were used.

Fetal heart sound (FHS) was recorded every half hourly and uterine contraction was monitored every half hourly after administration of drugs. Per vaginal examination were performed 4 hourly to assess the response of either drug to see the progress of labour. If women developed irregular FHS, women were kept in left lateral position with oxygen inhalation and intravenous fluid. Fetal condition was assessed by seeing the color of liquor and monitoring with CTG. In Group A, next dose of PGE2 was withheld and in group B, oxytocin infusion was stoppe. And if the FHS became regular, in Group A, next dose of PGE_2 was given and oxytocin infusion was restarted as before. If FHS persisted to be irregular then emergency cesarean section was done in both the groups. Outcome was observed in term of progress of labour i.e. onset of active stage and leaking to delivery interval in both the groups. After 1st dose, if the women in Group A went to active labour, then the next dose was withheld. Similarly in Group B women were monitored and dose of oxytocin was titrated according to the strength and number of contractions. Once women in active stage, progress of labour was monitored with Partograph. Failed Induction was defined as follows: Group A (PGE_2): If the women didn't go into active labour 6 hours after the 2nd dose, then the case was considered failed induction. Group B (Oxytocin): If the women didn't go into active labour after three subsequent pints of oxytocin (each dose of 5 U for primigravidae and 2.5 U for multigravidae), then the case was considered as failed induction.

RESULTS

Total 72 women with PROM were included in the study. Out of them 36 women received PGE_2 vaginal gel and 36 women received intravenous oxytocin for induction of labour. In PGE_2 group, 66.7% were primigravidae whereas in oxytocin group 58.3% were primigravidae (p value = 0.215). The period of gestation was 37 -40 weeks in 75% of the women in PGE_2 group and 80.5 % of the women in oxytocin group (p value = 0.156). Per speculum examination revealed pooling of liquor in posterior fornix in total 63 women; group A = 31 (86.1%), group B= 32 (88.9%). There were 4 women with soakage of pads in two hours observation period; group A = 1(2.8%), group B= 3(8.3%) and 5 women had membrane present with leaking PV; group A = 4(11.1%), group B= 1(2.8%). More women in group A (61.1 %, n= 22) had uneffaced cervix compared to group B (33.3%, n=12) (p value = 0.012). There was no significant difference in the mean pre-induction Bishop's score among the two groups (p value =0.251).

The time duration for induction to onset of active labour was similar in both the groups (Group A = 6.28± 3.01 hours, Group B = 5.54 ± 1.44 hours, p value = 0.273).

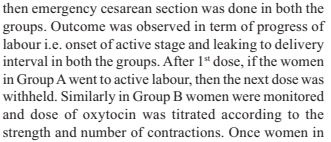

Fig 3. Induction to delivery interval

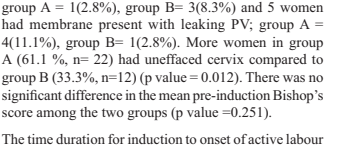

Fig. 4. Leaking to delivery interval

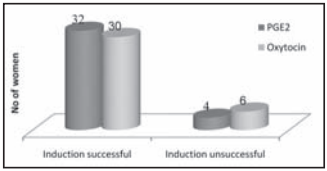

Fig. 5. Successful induction with PGE2 or oxytocin

Induction to delivery time was significantly high in PGE_2 group as compared to oxytocin group (Group A = 10.5 ± 4.88 hours, Group B = 6.90 ± 3.51 hours, P =0.002). There was no significant difference in leaking to delivery interval in both the groups (Group A = 14.97 ± 5.6 hours, Group B = 12.34 ± 4.86 hours, p value = 0.083). Most of the women in both the groups have succeeded in delivering within 18 hrs of leaking. There was no significant difference in the mode of delivery among the two groups (p value = 0.872). Majority of the women had vaginal delivery (group A= 32/36 group B =30/36). All the women (n=10) who had caesarean section were primigravidae and caesarean section rate was almost similar among PGE2 (11.1 %) and oxytocin group (16.7 %).

Statistical analysis showed no significant difference in indications for caesarean section among the two groups (p value =0.492). Failed induction accounted for 75 % of the LSCS in PGE2 group and 66.7% in oxytocin group. Induction was successful in 88.8%women with PGE_2 and in 83.3% in oxytocin group (p value = 0.063). Induction was successful with single dose of PGE_2 in 29 women (primi=20 and multi =9) and double dose was required in 7 women, all of them were primigravidae. Among the failed induction who had cesarean section, 3 out of 4 women were induced with 2 doses of PGE_2 gel, 1 out of 4 women had cesarean section for fetal distress after single dose. In group B the dose of oxytocin required for induction was 7327.41±6035.67 mIU in primigravidae and 4920.14 ± 3525.23 mIU in multigravidae.

Among 36 women in PGE_2 group, 3 women had hyperpyrexia and one woman had posterior vaginal wall tear whereas no maternal complications were noted in the oxytocin group. There was no significant difference in the APGAR score of newborn baby at 1 and 5 minutes in PGE_2 group compared with oxytocin group (Group A = 8.7±1.42, Group B=8.3±0.83, p=0.573). The rate of neonatal infection was not significantly different among the 2 study groups (p=0.375).

Table-1: Parity vs modes of delivery

		GE_2	Oxytocin	P value
Vaginal delivery	Primigravida	14	21	0.872
	Multigravida	18	9	
LSCS	Primigravida	4	6	
	Multigravida	0	0	

DISCUSSION

Premature rupture of membrane (PROM) at term is a common clinical problem, affecting roughly 8-10% of pregnant women. Spontaneous labor is expected to start within 24 hours of the rupture of fetal membranes in the majority of women. [2] However it may take longer time for onset of labour among the women who come with PROM and have low Bishops score increasing the risk of maternal, fetal or neonatal infection . Management of these women includes either expectant management or early induction of labour (active management).

Women managed expectantly will go into spontaneous labour and deliver within 24, 48 and 72 h of PROM in 70, 85 and 95 per cent of cases, respectively.[6,7] However the available evidence suggests that immediate induction of labor presents the most favorable outcome profile for pregnancies complicated by PROM at term. Immediate induction with oxytocin or PG offers significant benefits in terms of maternal infection when compared with expectant or delayed induction of labor. Studies have shown that immediate induction of labor is less likely to develop clinical chorioamnionitis and postpartum fever than those of expectant management or delayed induction.[1]

The conservative management may not be associated with increased risk for neonatal infection as long as the mother is not colonized with GBS.[8,9] However, no convincing benefit for expectant management has been found in well-designed randomized controlled trials. Thus, early induction of labor can be initiated to reduce the risk of maternal infection and shorten the delivery time in term pregnancies complicated with low Bishop Scores and PROM.[3,9]

Studies in the 1970s and 1980s reported higher rates of operative deliveries in women with term-PROM who were managed actively with induction of labor compared with expectant observation.[10,11] Later large, randomized, controlled trials found that labor induction with intravenous oxytocin was preferable in this group to expectant management or induction with PGE_2 gel, with no significant difference in the

rate of CS between the groups.[12,13] Although oxytocin is usually preferred to promote labor in term PROM, it was recently proposed that prostaglandins E_1 and E_2 can be administered vaginally to stimulate cervical ripening in term pregnancies complicated with low Bishop Scores and PROM.[14,15] PGE_2 is seen to be an effective agent that shortens the time from induction to delivery interval, improve success rates and reduce morbidity associated with labor induction. The present study describes results of management of women with PROM at term comparing use of iv oxytocin or intravaginal PGE_2 gel.

Similar study done by Kunt *et al*[3] had pre-induction Bishop score of 3.77 ± 1.1in PGE_2 group and 3.86 ± 1.5 0.72 in oxytocin group which is almost comparable to our study. They found that the time from labor induction to onset of active labor was significantly shorter in the oxytocin group than in the PGE_2 group (4.9 ± 4.1 *vs*. 8.5 ± 3.6 hours; $p = 0.02$). In this study, time interval to achieve active labour was similar in both the groups (Group A: 6.28± 3.01hrs, Group B: 5.54 ± 1.44 hrs , P value= 0.273).

Goeschen *et al* studied the influence of application of 0.4 mg prostaglandin E_2 (PGE_2) gel vs oxytocin on term pregnancies with premature rupture of the membranes (PROM) and unripe cervix.[16] They showed that induction to delivery interval was significantly reduced in PGE2 group. In contrast , Kunt et al found that the time from induction to delivery was significantly shorter in the oxytocin group (3.4 ± 1.5 *vs*. 9.6 ± 4.7 hours; $p = 0.02$).Our study also showed, induction to delivery time was significantly shorter in oxytocin group as compared to PGE_2 group (PGE 2: 10.5 ± 4.88 hours, Oxytocin: 6.90 ± 3.51 hours, P =0.002) . In this study, there was no difference in leaking to delivery interval in both the groups (Group A: 14.97 ± 5.63 hours, Group B: 12.34 ± 4.86 hours, p=0.083). However, Goeschen *et al* in similar study showed that PROM to delivery interval was significantly reduced in PGE2 group.[16] Chaudhuri *et al* observed that interval from induction to active labor, duration of active labor, and induction to delivery interval were not significantly different between the two groups.[17]

In the present study, the rates of cesarean delivery for the PGE_2 and oxytocin groups (11.1% and 16.7%, respectively) were similar. All the women (n=10) who had caesarean section were primigravidae. But, Chaudhuri *et al* observed that induction with PGE_2 resulted in significantly lower rate of cesarean section (17.8% vs 28.5%, P = 0.049) and operative vaginal delivery (3.5% vs 14.2%, P=0.007) among nulligravidae.[17] Their study had no significant difference in the mode of delivery among multigravidae. Grant *et al* demonstrated that PGE_2 significantly reduced the interval from PROM to delivery without causing any increase in cesarean rate.[18] Rhydstrom *et al* concluded that primigravidae with unfavorable cervix induced with oxytocin infusion had high cesarean section rate.[19] However, Kunt *et al* showed that vaginal administration of PGE_2 did not significantly affect the rate of cesarean delivery or indications.[3] The rates of cesarean delivery for the PGE_2 and oxytocin groups (20.0% and 18.3%, respectively) were similar in our study and the commonest indication for c-section was failed induction and this result is also comparable with the work of Rhydstrom and co-workers.[19]

The main concern related to PROM without uterine activity is the occurrence of maternal and neonatal infection because morbidity increases with a latent period of 24 hours. Grant *et al* and Conway *et al* recommended waiting for spontaneous onset of labor, especially in the presence of an unfavorable cervix.[18,20] Ahmed *et al* noted that most frequent maternal complications in PGE_2 group were vomiting, nausea and fever (12%).[21] Varma *et al* concluded PPH was less in PGE_2 group as compared to oxytocin group.[22,23] Chaudhuri *et al* showed that the maternal morbidity was almost negligible with the use of PGE_2 gel or iv oxytocin for induction of labour in term PROM. In their study, only a few neonatal infections occurred and no significant difference was noted between the two groups (2.7% vs 3.5%, P= 0.71).[17] In our study the maternal and neonatal outcomes were minimal and comparable in the two groups.

However in our study, incidence of fetal distress was similar in PGE_2 group (1/36) and oxytocin group (2/36). The APGAR score of newborn baby in PGE_2 group was comparatively better than oxytocin group in the study by Varma *et al*.[23] However, in our study there was no significant difference in the APGAR score of newborn baby in PGE_2 group compared with oxytocin group (p=0.573). Similarly, the rate of neonatal infection was not significantly different among the 2 study groups (p=0.375).

Our study shows that intravaginal PGE_2 and iv oxytocin are both effective and safe in induction of labour in term PROM at term. There is no significant difference in maternal and fetal outcomes. The duration of hospital stay and leaking to delivery interval are comparable, though induction to delivery interval is significantly high in PGE_2 group as compared to oxytocin.

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