

## Comparison of the Response of Oxytocin Versus Prostaglandin E<sub>2</sub> Vaginal Pessary for Labour Induction in Prelabour Rupture of Membranes

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**Objective:** To compare the response of oxytocin versus prostaglandin E<sub>2</sub> vaginal pessary for labour induction in prelabour rupture of membranes at term in primigravida patients with poor Bishop score.

**Design:** It was a prospective comparative study.

**Setting:** The study was conducted in the department of Gynae & Obs, Ittefaq hospital (Trust), Lahore during a period of one year i.e from July 2007 to June 2008.

**Patients and Methods:** Fifty primigravidae with prelabour rupture of membranes at term having Bishop score < 5 or 5 were randomized into 2 groups to undergo induction of labour with either oxytocin or prostaglandin E<sub>2</sub> vaginal pessary. Main outcome measures were induction-initiation of labour interval, induction-delivery interval, maternal complications during induction, mode of delivery, fetal outcome and total hospital stay.

**Results:** The induction-initiation of labour interval (P=0.005), duration of improvement in Bishop score, induction-delivery interval (P=0.011) and total hospital stay (P=0.018) were shorter in PGE<sub>2</sub> induced patients. Moreover, majority of the patients delivered vaginally, had no maternal complications, did not require augmentation of labour, had less evidence of fetal distress (P=0.011) and better APGAR score at birth in this group. Majority of the neonates in the 2 groups did not require admission in neonatology unit (P=0.666).

**Conclusion:** Prostaglandin E<sub>2</sub> vaginal pessaries are very safe and effective to stimulate labour with ruptured membranes and poor Bishop score.

### 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.<sup>1</sup>

Rupture of membranes is when chorioamniotic membranes break and release amniotic fluid. Prelabour rupture of membranes (PROM) is defined as rupture of membranes with a latent period before the onset of spontaneous uterine activity. Its significance lies in the fact that it has obscure etiology with difficulties in diagnosis and is associated with significant maternal and neonatal risks.<sup>2</sup>

PROM occurs in 10% of all pregnancies with majority of cases (60-70%) occurring before 37 completed weeks of gestation. Its incidence generally varies between 2-18%.

Infections of lower genital tract and amniotic cavities are most common etiologies of PROM.

Risks of PROM include risk of sub-clinical chorioamnionitis, increased likelihood of operative delivery, increased incidence of marginal cord insertion and battle door placenta which itself is associated with retained placenta and both primary and secondary postpartum hemorrhage. Risk of abruption-placentae is 4-7%, postpartum endomyometritis is 10% and there is also risk of maternal pyelonephritis.

Reported incidence of neonatal sepsis is 2-4%.<sup>3</sup> Fetal hypoxia may occur due to cord prolapse, cord compression

and abruption-placentae. Due to reduced volume of amniotic fluid, mechanical difficulties may occur in delivery resulting in neonatal morbidity.

The management strategies of PROM at term are diverse and controversial.<sup>4</sup> Despite the extensive research and studies done in this field, there is still no universally accepted policy for the management of PROM at term and management varies between immediate induction and awaiting a certain period of time.<sup>5-7</sup> After 36 weeks, expectant management policy may be justified initially because it can be anticipated that 75-85% of these women will labour within 24 hours<sup>8</sup> and risk of caesarean section may be lower. Also, there is decreased risk of instrumental vaginal delivery and no significant increase in maternal or neonatal morbidity.<sup>9</sup>

The controversial aspect of expectant management is high risk of maternal and neonatal infection as the latent period lengthens along with increased risk of umbilical cord compression and abruption-placentae. However, the main aim should be to deliver the baby before the signs of chorioamnionitis appear.<sup>10</sup>

Expectant management also prolongs hospital stay and may be associated with worsening of perinatal outcome.<sup>11,12</sup> This has to be compared with the risks of induction of labour. The decision is best made with the couple after discussing the risks and benefits of two approaches and a mutually acceptable treatment plan is developed.

So the question arises which is the most suitable agent to induce labour? Various pharmacological techniques have been used for cervical ripening and labour induction<sup>13-15</sup> but only a few have been scientifically evaluated. Intravenous injection of Oxytocin, use of relaxin and estrogen are the methods tried. Now, different preparations of prostaglandins have been used<sup>16</sup> but the effectiveness of all these agents is still questionable.<sup>17,18</sup> There are very few prospective randomized studies to assess the efficacy of oxytocin and prostaglandin E<sub>2</sub> vaginal pessary for labour induction in primigravidae at term with poor Bishop Score and PROM.

This comparative study was conducted in an attempt to reduce the maternal and neonatal morbidity due to complications of PROM and to improve maternal and fetal outcome. The results of this study will help in making a definitive assessment plan for these patients so that the risks of maternal, fetal and neonatal morbidity and mortality are reduced.

### Materials and Methods

This cross-sectional study was conducted in the Department of Obstetrics & Gynaecology, Ittefaq Hospital (Trust), Lahore. Sixty primigravidae with PROM were randomized into two groups to undergo induction with oxytocin and prostaglandin E<sub>2</sub> vaginal pessary. The patients selected were those who had spontaneous rupture of membranes for < 24 hours at term, were afebrile with no evidence of fetal distress, having cephalic presentation, singleton pregnancy, adequate pelvis, having no obstetrical or maternal indication for cesarean section and Bishop score < 5 or equal to 5. Patients with intrauterine fetal demise were also included in the study.

Patients excluded from the study were those who had history of labour pains, previous uterine surgery, with known hypersensitivity to prostaglandins and having congenitally abnormal babies. The procedure was explained in detail to the patients and written consent was taken. Detailed history was taken regarding rupture of membranes. Detailed general physical and systemic examination was carried out noting particularly temperature, pulse, uterine tenderness and engagement of fetal head. Obstetrical ultrasound was carried in each patient to confirm gestational age, to assess the amount of liquor and to rule out congenitally abnormal babies.

Diagnosis was confirmed by per speculum and vaginal examinations. Bishop score was assessed and cord prolapse was excluded. Half of the patients were induced with prostaglandin E<sub>2</sub> vaginal pessary and other group with intravenous oxytocin diluted in Ringers Lactate. Its dose was adjusted according to uterine response intermittently. Intravenous antibiotics were started. Data was collected using a structured questionnaire.

Maximum of three vaginal pessaries were inserted at the interval of 6 hours if there was no improvement in Bishop score and labour was not started. In oxytocin induced group, dose was increased accordingly.

In order to detect the signs of infection in mother and fetal distress, maternal monitoring was done by 4 hourly pulse and temperature record, palpation of abdomen to detect uterine tenderness, noting the colour and smell of liquor and intermittently recording fetal heart rate.

Success of induction was declared when effective uterine contractions were started along with improvement in Bishop score. Labour was then augmented if required. If there was failure to induce labour in 24 hours, or evidence of maternal or fetal compromise, caesarean section was done. Antibiotics were given to babies after delivery with evidence of chorioamnionitis. Neonates were admitted in neonatology ward with poor Apgar score. Total hospital stay was noted. Observations for signs of infection were continued in puerperium.

### Results

At the end of the study, all gathered data in questionnaire was tabulated. The variables analyzed at the end of the study were induction-initiation of labour interval, induction-delivery interval, maternal complications and fetal distress during induction, total hospital stay, mode of delivery, fetal outcome and need for augmentation of labour. Data was presented as frequencies, proportions and means. The 2 means were tested using a t-test and the 2 proportions by Chi-square test at an alpha level of 0.05 in 2 tails.

Mean age (+ SD) among patients undergoing induction with oxytocin (Group 1) and PGE<sub>2</sub> vaginal pessary (Group 2) was 22.28 + 2.99 and 24.12 + 2.52 years respectively. Mean (+ SD) duration of rupture of membranes between 2 groups was 7.52 + 3.49 and 5.76 + 3.39 hours respectively.

The mean induction-initiation of labour interval among 2 groups was 3.16 + 2.32 and 1.72 + 0.79 hours respectively (P = 0.005) (Table 1).

Majority of the patients (40%) in Group 2 had improvement in Bishop score within 2 hours of start of induction. In group 1, majority (40%) of the patients had no improvement in Bishop score in this period. Rather, after 3-4 hours, only 24% of the patients showed improvement in Bishop score in Group 1.

Majority of the patients in group 2 (84%) had spontaneous vaginal delivery. In group 1, 13 patients (52%) delivered vaginally while remaining 12 (48%) by caesarean section (P = 0.032). The commonest indication was failed induction in this group.

In majority of the patients in Group 2 (68%), no maternal complications were noted during induction. In the remaining patients in this group, vomiting and fever (12% each) were the most common complications encountered while nausea and primary postpartum haemorrhage were least commonly seen (4% each). In the oxytocin induced group, majority of the patients developed fever during induction (40%). Eight of them developed no complications (32%) while 4 (16%) had vomiting and 3 (12%) had nausea as the sole complication.

Labour was augmented in majority of the patients (80%) in group 1. It was not needed in most of the patients (56%) in group 2 ( $P = 0.019$ ) and is significant.

The mean (+ SD) induction-delivery interval in group 1 and 2 was  $11.38 + 4.31$  and  $7.43 + 4.08$  hours respectively ( $P = 0.011$ ) and is significant (Table 2).

Mean (+ SD) number of patients showing any evidence of fetal distress among the two groups were  $11.38 + 4.3$  and  $7.43 + 4.08$  respectively ( $P = 0.011$ ) and is significant.

The mean (+ SD) APGAR score of the newborn babies immediately at birth in 2 groups is  $5.16 + 1.46$  and  $6.24 + 1.4$  respectively ( $P = 0.014$ ).

The mean (+ SD) hospital stay among patients of two groups was  $3.36 + 2.33$  and  $1.92 + 1.08$  days respectively ( $P = 0.018$ ) and is significant (Table 3).

Majority (88%) of the neonates in the 2 groups did not need admission in neonatology unit ( $P = 0.666$ ) and is not significant. Only two babies were admitted for 2 days and 1 baby was admitted for one day only in both groups.

Induction of labour was successful in majority of the patients (84%) in group 2. It was roughly successful in half of the patients (52%) in group 1 while unsuccessful in remaining half (48%).  $P$  value is 0.016 and is significant.

## Discussion

The management of PROM at term is still a matter of debate and varies from centre to centre. On literature search, very few studies are available which compare effectiveness of Oxytocin and prostaglandin E<sub>2</sub> vaginal pessary for induction of labour in such patients. Further, these studies do not compare all the variables associated with labour and delivery. This study is with a small sample size and the results cannot be generalized for the whole population. However, it is expected that these results will not be very much different if a study is done with a probability sample for the whole city.

In my study, majority of the patients (84%) induced with PGE<sub>2</sub> vaginal pessary had spontaneous vaginal delivery while only 16% were delivered by cesarean section. This is comparable with the study of Varma TR<sup>19</sup> and his colleagues who concluded that PGE<sub>2</sub> treated patients had fewer cesarean sections for failed induction and high rates were associated with oxytocin. Similarly, cesarean section rate in labour induced by oxytocin is upto 30% which is close to my study. Another study by Rhydstrom and his colleagues<sup>20</sup> concluded that nulliparae with unfavourable cervix induced with oxytocin infusion had high cesarean section rate. In another study by Kelly and his colleagues, it was found that oxytocin alone was associated with an increase in unsuccess-

**Table 1: Induction-initiation of labour interval.**

Time (Hrs)	PGE <sub>2</sub> vaginal pessaries		Oxytocin	
	N = 25		N = 25	
	Number	Percentage	Number	Percentage
1 – 2	20	80.0	13	52.0
3 – 4	5	20.0	08	32.0
5 – 6	-	-	02	08.0
> 6	-	-	02	08.0
<b>Total</b>	25	100	25	100.0
<b>Mean + SD</b>	<b>1.72 + 0.79</b>		<b>3.16 + 2.32</b>	
<b>P Value = 0.0005 (significant)</b>				

**Table 2: Induction-Delivery Interval.**

Time (Hrs)	PGE <sub>2</sub> Vaginal Pessary		Oxytocin	
	N = 21		N = 13	
	Number	Percentage	Number	Percentage
2 – 4	6	28.57	-	-
5 – 7	6	28.57	4	30.77
8 – 10	3	14.29	2	15.38
11 – 13	5	23.81	4	30.77
> 14	1	04.76	3	23.08
<b>Total</b>	<b>21</b>	<b>100.0</b>	<b>13</b>	<b>100.0</b>
<b>Mean +SD</b>	<b>7.43 + 4.08</b>		<b>11.38 + 4.31</b>	
<b>P Value = 0.011 (significant)</b>				

ful vaginal delivery within 24 hours.<sup>21</sup> In this study, the commonest indication for c-section was failed induction and this result is also comparable with the work of Rhydstrom and co-workers.

The most frequently noted maternal complications in this study in PGE<sub>2</sub> group were vomiting, nausea and fever (12%) while postpartum hemorrhage was least commonly seen. These results are comparable with the results of Leug and his colleagues<sup>22</sup> who found that in PGE<sub>2</sub> users, there was a trend towards lesser blood loss in delivery. Similar results were also obtained in the study by Varma and his colleagues who concluded that in PGE<sub>2</sub> users, there were fewer postpartum hemorrhages. Similarly, in a study by Ray and Garite,<sup>23</sup> there was statistically significant decrease in the incidence of chorioamnionitis in PGE<sub>2</sub> users as compared to oxytocin group which is comparable to my study.

In this study, the induction to initiation of labour interval was shorter in PGE<sub>2</sub> group as compared to oxytocin group which is comparable with the work of Ratnam and his colleagues<sup>24</sup> in the department of Obstetrics and Gynaecology, National University Hospital, Singapore who con-

cluded that use of PGE<sub>2</sub> pessary resulted in more women establishing labour earlier with a resultant reduction in admission to delivery interval. In this study, the induction to delivery interval was shorter in PGE<sub>2</sub> users as compared to oxytocin group. This is consistent with the work of Lettau and his colleagues<sup>25</sup> who concluded that use of prostaglandins for induction of labour seems to be recommendable measure as it is associated with shorter induction to delivery time.

In this study, in 80% of the patients induced with oxytocin, labour was augmented which was less frequently required in PGE<sub>2</sub> users. This result is comparable with the results of Lane and his colleagues<sup>26</sup> who found that if augmentation is required in PGE<sub>2</sub> group, the maximal concentration of oxytocin used and duration of use at this concentration was significantly less than in oxytocin group.

The patients who developed fetal distress was significantly less in PGE<sub>2</sub> group than oxytocin group. Similar results were obtained in the study by Cowell and his colleagues as PGE<sub>2</sub> induced patients had fewer cesarean section rates due to fetal distress. Also Rhydstrom and his colleagues found that nulliparae with unfavourable cervix at admission induced with oxytocin had high rate of ominous fetal heart rate findings and hence high cesarean section rate (20). Similarly in a study by Hannah and colleagues, it was concluded that induction of labour by oxytocin increased the need of internal fetal heart monitoring due to increased risk of fetal distress during induction.

The Apgar score of newborn baby in PGE<sub>2</sub> group is comparatively better than oxytocin group in my study which is consistent with the work of Varma and co-workers<sup>19</sup> in which incidence of infants with low Apgar score was also significantly less.

Majority of the neonates did not need admission in neonatology unit in this study in two groups. This is comparable with the work of Ratnam<sup>23</sup> who concluded that there were no significant differences in neonatal outcome in 2 groups. The rate of neonatal infection was not significantly different among the 2 study groups in another study by Hannah et al. However, this is in contrast to the work done by other researchers who concluded that induction with PGE<sub>2</sub> pessaries increases the risk of neonatal infection compared to induction with oxytocin and also increase the need of neonatal antibiotic therapy and admission to neonatal intensive care for > 24 hours. This can be explained by the fact that all patients in this study received prophylactic antibiotics during induction with close surveillance for any sign of infection in the mother and careful monitoring of fetal heart rate with avoidance of unnecessary digital vaginal examinations during labour hence reducing the possible risk of neonatal infection and subsequent admission in neonatology.

### Conclusion

The management of PROM at term is still questionable and varies from one centre to another between expectant and

active management. Overall, the comparison of oxytocin alone with either intravaginal or intracervical prostaglandin E<sub>2</sub> reveals that these agents have probably more benefits than oxytocin alone for induction of labour when spontaneous rupture of membranes has occurred in the absence of uterine contractions and with poor Bishop score. However, still to-date, the amount of information relating to specific clinical sub-groups is limited and awaits further research.

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