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OXYTOCIN ALONE VERSUS DINOPROSTONE INSERT FOLLOWED BY OXYTOCIN FOR INDUCING LABOUR IN TERM PRELABOUR RUPTURE OF MEMBRANES

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Abstract:

Introduction: Immediate induction in Term Prelabour rupture of membranes (PROM) decreases infectious morbidity in mother and baby. Induction of labour in Term PROM with unfavourable cervix can be done directly with oxytocin or by first priming the cervix with prostaglandins followed by oxytocin augmentation if needed. Direct oxytocin induction leads to shorter induction to delivery interval but increases caesarean delivery.

Objective: To compare the induction to delivery interval and feto-maternal outcome in women with Term PROM and unfavourable cervix induced with Oxytocin versus Dinoprostone (PGE2) Vaginal insert followed by oxytocin.

Methods: This was a randomized comparative study including 150 low risk pregnant women with term PROM and poor bishops score, done over a period of 18 months, women were randomized into 2 groups of 75 each after obtaining informed consent. Women in group-A were induced with Oxytocin directly while Group-B were first primed with dinoprostone vaginal insert followed by oxytocin induction/augmentation if needed. All women were followed for induction to delivery interval and feto-maternal infectious morbidity.

Results: Induction to delivery interval and hospital stay was significantly shorter in group A as compared to group B, 11.4 hours & 18.3 hours, $p < 0.001$ and 75.12 hours & 90.48 hours, $p < 0.001$ respectively. The caesarean rate was similar in both groups, $p=0.546$. There was no feto-maternal infectious morbidity in the study population.

Conclusion: Direct oxytocin induction in term PROM results in shorter induction delivery interval and shorter duration of hospital stay without increasing caesarean rate.

Keywords: Term PROM, Induction of labour, Oxytocin augmentation, dinoprostone vaginal insert, bishops score, induction to delivery interval.

Introduction

Prelabour rupture of membranes (PROM) is the rupture of amniotic membranes prior to onset of labour and occurs in approximately 10% of pregnancies. [1] It can occur at term (≥37 weeks of pregnancy) or preterm (< 37 weeks of pregnancy). At least 80% of cases of PROM occur at term. [2]

Ruptured membranes are the end result of a combination of programmed cell death. Activation of catabolic enzymes like collagenase, and mechanical forces due to uterine contraction lead to rupture of membrane before onset of labour. [3] Patients with PROM present with complaints of sudden watery leakage and the diagnosis is confirmed by visualization of amniotic fluid passing from the cervix during speculum examination. Other diagnostic tests for women without clearcut visualization of amniotic fluid at the time of per-speculum examination include ferning of dried amniotic fluid (AF) on microscopic examination, alkaline pH of amniotic fluid as evaluated by Nitrazine paper and decreased amniotic fluid on ultrasonographic examination. [4]

The loss of protective amniotic membranes exposes the sterile intrauterine environment to ascending infections from cervicovaginal flora. An unfavourable cervix is seen in up to 40% of patients diagnosed with term PROM. Management of patients with term PROM, particularly those who have an unfavourable cervix, remains controversial. The main controversy in the management of these patients is whether the patient should be allowed to enter into labour spontaneously by following expectant management for 24 hours or to actively induce labour.

Expectant management has been linked to an increase in maternal and new born infectious morbidity due to longer time to delivery, while immediate induction, due to a shorter period between the PROM and birth, reduces the risk of maternal and neonatal infections, but can increase caesarean delivery rates. [6]

The choices in cases of unfavourable cervix are either immediately inducing labour directly with oxytocin or first ripening the cervix with prostaglandins. [6] Cervical ripening using prostaglandins in PROM is preferred as use of mechanical methods like laminaria tent or foleys catheter is linked with increased infection rates. [6,7] In India, Dinoprostone vaginal insert available for vaginal use as a 10 mg PGE2 insert releasing prostaglandin at a rate of 0.3 mg an hour is the only available option as oral/vaginal misoprostol is not approved by DGCI. [6]

While the specific mechanism of action is uncertain, prostaglandin E2 stimulates the myometrium contractions directly. It binds to EP1-4 G protein-coupled receptors (GPCRs), which trigger a number of downstream events depending on the subtype of EP and cell type specific expression patterns. [7]

There is no consensus on the management of women with term PROM who choose to undergo induction of labour with unfavourable cervix. Use of Dinoprostone vaginal insert for cervical ripening before induction of labour using oxytocin has not been observed to be superior to the use of oxytocin alone. Thus, there is a need to identify the most appropriate method for induction of labour in women with term PROM admitted with unfavourable cervix. This study was planned to compare induction to delivery interval, mode of delivery and feto-maternal infectious morbidity with the use of oxytocin directly versus first priming the cervix with dinoprostone vaginal insert followed by oxytocin for induction of labour in women with term PROM.

Materials and Methods

This was a randomized comparative study conducted on 150 women with Term PROM with an unfavorable cervix admitted in the obstetric ward over a period of 18 months in a tertiary care hospital. The sample size was calculated based on the observation that rate of vaginal delivery within 24 hours of labor induction was 63.3% in direct oxytocin infusion group as compared to 78.5% in the dinoprostone followed by oxytocin infusion group. [9] Taking these values as reference, the minimum required sample size with 80% power of study and 5% level of significance is 137 patients in each study group. For finite sample size taking population as 200, total sample size calculated was 116. To reduce margin of error, total sample size taken is 150 (75 patients per group). Before starting study, ethical clearance was taken from Institutional Ethical committee and CTRI registration number was obtained.

Women with singleton, term, live pregnancy (37 to 40 weeks gestation) admitted in obstetric wards with PROM, not in labour and willing to participate in the study, were screened. Women with

multifetal gestation, fetal distress, signs of infection, favourable cervix (Bishop score >6), previous caesarean and medical or obstetric comorbidities were excluded from the study.
Women who met inclusion criteria were monitored for one hour to determine that there was no spontaneous onset of labour and maternal infection. Fetal well-being was documented with admission cardiotogography (CTG).
After taking written informed consent, women were randomly allocated to the two treatment arms by the sequential opening of sealed, numbered envelopes. Group A comprised of 75 women allotted to direct induction with oxytocin infusion and Group B comprised of 75 women allotted to priming with Dinoprostone (PGE2) Vaginal insert (Propess) and if needed followed with induction /augmentation with intravenous oxytocin infusion.
Women in group A recieved oxytocin by infusion pump, started at 2miu/min and exponentially increased every 30 minutes till a maximum dose of 32 miU/min for multigravida and 64 miU/min for primigravida was infused or till 3-4 contractions were achieved in a 10-minute interval. Oxytocin infusion was continued till 1 hour after delivery unless otherwise indicated.
Women in group B had cervical priming with Dinoprostone (PGE2) Vaginal insert (Propess). Dinoprostone Vaginal insert was stored in freezer and was taken out of freezer just prior to insertion. Taking aseptic precautions, the vaginal insert was inserted in posterior fornix, in transverse orientation. Women were asked to be recumbent for 30 minutes after instillation of Dinoprostone vaginal insert. It was removed when 3-4 uterine contractions each lasting for 30 to 40 seconds over 10 minutes started, irrespective of any cervical change, or after 24 hours irrespective of contractions. Labour was induced/ augmented with oxytocin 30 minutes after removal of PGE2 vaginal insert.
As per our hospital protocol all the women in the study with leaking per vaginum for >18 hours received Inj. Ampicillin 2 gm stat followed by 500mg 6 hourly, Inj. metronidazole 500 mg IV 8 hourly and Inj.Gentamicin 80 mg IV 12 hourly till delivery and for 72 hours post-delivery.
All the women and neonates were followed for infectious morbidity. The main outcome recorded was mode of delivery. Other outcomes noted were, Induction to delivery interval, Maternal Infectious Morbidity (Chorioamnionitis/Sepsis/Endometritis), Length of hospital/ICU stay and Fetal outcome (NICU admission due to Sepsis). The data was entered in MS EXCEL spreadsheet and analysis was done using Statistical Package for Social Sciences (SPSS) version 21.0.

Results

A total of 150 women with Term PROM and unfavourable cervix were included in the study, 75 in each group. The mean age, parity, education, employment and period of gestation of women in both groups were comparable. (Table: 1)
The duration of induction to delivery interval was significantly shorter in women in group A as compared to women in group B, 11.4 ± 6.5 hrs & 18.3 ± 6.6 hrs, respectively, P <0.001. There were no women with abruption in group A, whereas 6 women in group B developed blood-stained liquor, the occurrence of abruption in group B was statistically higher, P=0.013. Rate of foetal distress (non-reassuring foetal heart and meconium-stained liquor) in both groups was similar. (Table: 2)
Most women in both groups delivered vaginally, the mode of delivery in both groups was comparable. Twelve (8.0%) women had caesarean delivery, 7 (9.33%) in group A of which 3 were for failed IOL, 2 for arrest of dilatation, and 2 for foetal distress. In group B, 5 (6.66%) women had caesarean delivery of which 3 were for foetal distress and 2 were for arrest of dilatation. The caesarean delivery rate was similar in 2 groups, P=0.547. (Table: 2)
There was no significant difference in NICU admission in both the groups 4 (5.3%) & 5 (6.7%) respectively, P=1.000. None of the study participants (n = 150) were found to have any infectious morbidity. The duration of hospital stay was significantly shorter in group A as compared to group B, 3.13 ± 0.38 days & 3.77 ± 0.56 days P<0.001. (Table: 2)

Discussion:

A longer time interval between the rupture of membranes and the commencement of labor leads to increased risk of ascending infection and the development of chorioamnionitis. [4] As the time interval between the rupture of membrane and the delivery exceeds 24 hours, the risk of chorioamnionitis increases five-fold, and risk of neonatal infections also increases.

Expectantly managed Term PROM are followed by commencement of spontaneous labor within 24 hours in 70% cases, while 85% go into labour within 48 hours and 95 percent will do so within 72 hours. [2] Women managed expectantly have increased risk of cord compression, cord prolapse, and abruptio placenta. Therefore, many international societies have recommended immediate induction of labour in patients of term PROM. [9,10,11] However, ACOG and RCOG recommend offering a choice between immediate induction and expectant management up to 12 to 24 hrs. [2,10] Hagen ID et al observed more infectious morbidity in term PROM cases managed expectantly as compared to those undergoing immediate induction, 7.53% and 5.55%, respectively.[12] Also, Cochrane database of systematic reviews in 2017 reported a clear reduction in infection morbidity for the planned early birth group compared with the expectant management group. [5]

As conservative management of term PROM requires in-patient care for close follow up and is associated with prolonged hospital stay, to manage term PROM, we follow a policy of immediate induction of labour.

Various agents have been used to induce labour in term PROM with poor bishop's score. Prostaglandins in different formulations like oral/vaginal misoprostol, dinoprostone as vaginal gel/pessary have been advocated for cervical ripening. [10,11,13,14] However, direct oxytocin induction has been reported to be more effective. [2,11]

We conducted this study on 150 women with term PROM, to compare direct oxytocin infusion with priming with prostaglandins before starting oxytocin. We observed shorter induction- delivery interval and shorter hospital stay in women induced directly with oxytocin. Similar results were observed in other studies conducted by Güngördük K et al, Kulhan NG, and Kunt C et al. [9,16,17] This is because the uterus is sensitive to oxytocin at term due to up regulation of the myometrial oxytocin receptors caused by high estrogen levels in late pregnancy. [15]

Similar to other studies, we observed no significant difference in the mode of delivery between the two groups. [9,16,17] Induction was equally successful by both methods and most of the women delivered vaginally, 90.66% in Group A and 93.33% in Group B. In Group A only 3 patients had caesarean section for failed induction while none in direct oxytocin group had caesarean section for failed induction. Foetal distress as an indication for caesarean delivery was seen in only 5 (3.33%) cases. This is in contrast to other studies by Kulhan NG and Kunt C et al where caesarean section for foetal distress was done, 29 cases (12.9%) and 28 cases (11.66%) respectively. [16,17]

None of the women in the study population had any infectious morbidity. Kunt C et al in 2010 also did not find any cases of intrapartum chorioamnionitis or postpartum endometritis in their study population of 240 women. [17] Although, Kulhan NG 224 women and Güngördük K et al observed infectious morbidity (chorioamnionitis & endometritis) in their study population, the difference between women undergoing direct oxytocin infusion and cervical primming before oxytocin, was not statistically significant. [9,18] The reason for not having any infectious morbidity in our study population could be a smaller sample size and routine use prophylactic broad-spectrum antibiotics in women with more than 18 hours of leaking, according to institutional protocol.

Conclusion:

Women with term PROM, undergoing induction directly with oxytocin without priming of cervix with dinoprostone vaginal insert have a shorter induction to delivery interval without significantly increasing the caesarean delivery rate. The total duration of hospital stay is also shorter in these women.

Also, oxytocin is cheap, easily available and can be easily stored as compared to dinoprostone vaginal insert. Therefore, direct oxytocin induction is more cost effective and suitable in a low resource setting as an effective treatment option in term PROM cases with unfavourable cervix.

Table 1: DEMOGRAPHIC CRITERIA

	Group A (n=75)	**Group B (n=75)**	**P value**	**Test performed**
AGE (years) <25	43 (57.3%)	42 (56.0)	0.869	Fisher Exact test
PARITY Primi	52(69.3%)	59(78.7%)	0.193	Fisher Exact test
EDUCATION Literate	28(37.33%)	22(29.33%)	0.154	Fisher Exact test
EMPLOYMENT Employed	10(13.33%)	7(9.33%)	0.167	Fisher Exact test
POG AT DELIVERY 37 WEEKS 38 WEEKS 39 WEEKS 40 WEEKS	 33(44.0%) 19(25.3%) 18(24.0%) 5(6.67%)	 23(30.7%) 31(41.3%) 14(18.7%) 7(9.3%)	0.186	Chi Square test

Table 2: CLINICAL OUTCOMES

	Group A (n=75)	**Group B (n=75)**	**P value**	**Test performed**
Induction to delivery interval (in hours) Mean ± SD	11.4 ± 6.5	18.3 ± 6.6	**<0.001**	T test
Non reassuring FHR	8(10.7%)	10(13.33%)	0.264	Fisher Exact test
Mode of delivery LSCS	7 (9.3%)	5 (6.7%)	0.547	Fisher Exact test
Liquor Blood stained Meconium stained	 0 (0.0%) 9 (12.0%)	 6 (8.0%) 13 (17.3%)	**0.013**	Fisher Exact test
Maternal PPH	1 (1.3%)	2 (2.7%)	1.0	Fisher's exact test
APGAR score >7	2(2.7%)	0(0%)	0.4966	Fisher's exact test
NICU ADMISSION	4(5.3%)	5(6.7%)	1.0	Fisher's exact test
Infectious Morbidity (Endometritis/ Chorioamnionitis/Sepsis)	0	0	-	-
Duration of hospital stay (in days)	3.13 ± 0.38	3.77 ± 0.56	**<0.001**	T test

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