Original Research Article

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Term PROM : Induction of Labour By Dinoprostone Followed by Oxytocin Versus Oxytocin Alone

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Abstract

Context: Pre labour rupture of membrane (PROM) is a common event in obstetrics.There is still controversy regarding the best method of induction of labour. So purpose of this study is to verify the efficacy and safety in between the two methods of induction i.e. oxytocin alone or dinoprostone followed by oxytocin. *Aims:* Comparison of efficacy of oxytocin versus dinoprostone gel followed by oxytocin for induction of labour in PROM in terms of induction delivery interval, mode of delivery and maternal & fetal outcome. *Settings and Design:* This study was carried out at a tertiary care hospital. Admitted women from the labour ward and obstetric wards were enrolled in the study after taking written informed consent. *Material and Methods:* Randomized control study in a tertiary care hospital and referral centre for one year. Two hundred women randomly allocated to study group A & control group B after fulfilling inclusion/ exclusion criteria. Group A patients were induced with dinoprostone gel 0.5 gm followed by oxytocin six hours later. Group B patients were induced with oxytocin alone. *Results:* There was no difference in mean induction to delivery interval of both groups. Proportion of vaginal delivery in Group A was significantly higher than that of Group B because of higher proportion of failed induction and non progress of labour in later. There was no significant difference in maternal and fetal outcome in both the groups. *Conclusion:* Study showed that use of sustained released dinoprostone followed by oxytocin for induction of labour in term PROM led to a significantly higher proportion of women with vaginal delivery within 24 hours of induction, and a small proportion of women who required cesarean section compared with the use of oxytocin alone.

Keywords: Premature Rupture of Membrane (PROM); Oxytocin; Dinoprostone.

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Introduction

Pre labour rupture of membrane (PROM) is a common and important event in obstetrics. In approximately 8% of women with pregnancies at term, the fetal membranes rupture before labour begins. Spontaneous labour follows term PROM at 24, 48 and 96 hours in 70%, 85% and 95% of women, respectively. Thus, an important proportion of women have significant latency from PROM to delivery if managed expectantly, particularly nulliparous women [1]. And as the time between the rupture of membranes and the onset of labour increases, so may the risk of maternal and fetal infection [2]. Modern obstetrics aims at improving the safety of the mother and the fetus throughout antenatal period as well as parturition. For this reason, many physicians recommend that labour be induced if the pregnancy is at term and labour does not begin

spontaneously shortly after the membranes rupture. If the labour is induced, the methods of induction are usually by intravenous administration of oxytocin, vaginal/cervical prostaglandins or vaginal/oral misoprostol. More recently, prostaglandins, followed by an infusion of oxytocin, if necessary have been used. There is still controversy regarding the best method of induction of labour. So purpose of this study is to verify the efficacy and safety in between the two methods of induction i.e. oxytocin alone or dinoprostone followed by oxytocin.

Materials and Methods

This randomized control study was carried out at a tertiary care hospital and referral centre from Jan 2013 - Dec 2013 after obtaining permission from Institutional Ethics Committee. Admitted women from the labour ward and obstetric wards were enrolled in the study after taking written informed consent. The women were randomized into two groups. Total number of 200 women were included and randomly allocated to the study group A and control group B, after fulfilling inclusion/exclusion criteria. Study group A included 100 women who were induced with dinoprostone gel 0.5 mg followed by oxytocin 6 hours latter. Comparative group B included 100 women who were induced with oxytocin alone.

Inclusion Criteria

1. Pregnant women with ruptured membranes
2. Gestational age (GA) of 37 -42 weeks
3. Single live fetus
4. Cephalic presentation
5. Adequate pelvis
6. Reactive fetal heart rate on Non-Stress Test (NST).
7. Bishop's score ≤ 5

Exclusion Criteria

1. Patient is in labour
2. Contraindication for expectant management (e.g.: meconium stained liqour)
3. Duration since rupture of membrane is >24 hours or chorioamnionitis
4. Post cesarean or any previous uterine surgery
5. Cephalopelvic disproportion
6. Hypersensitivity to prostaglandins
7. History of asthma, allergy or glucoma
8. Para >2

On admission,apart from patient particulars, thorough general examination and systemic examination was carried out. Diagnosis of PROM 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. 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 group. Randomization was done using a table of random numbers. Labour monitoring was done using partograph. Reactive NST was confirmed before induction.

Procedure

Group A: Under all aseptic precautions, vulva and vagina was cleaned and 0.5 mg PGE2 (Cerviprim®, Astra ZenecaTM) net weight 3 gm, prepacked in the sterile prefilled ready-to-use syringe was introduced intracervical (In cases of active dribbling, it was given in the posterior fornix). If labor had not supervened after 6 hours application of PGE2 gel was repeated. Vaginal examination repeated every 6 h and progress noted with Bishop score. At the end of 12 h, if the women has still not set into labor it was labeled as failed induction. But if bishop score was found to have changed by ≥ 2 and if indicated, oxytocin drip was started.

Group B: Induction of labor with an oxytocin infusion was done. One unit of oxytocin were placed in 500 ml of Ringer's lactate and the infusion started at 2 mIU/minute (15 drops/min). The oxytocin infusion rate was doubled every 20-30 minutes until three contractions were obtained in 10 minutes or until a maximum infusion rate of 32 mIU/minute (which was achieved by adding 4 units in 500ml of Ringer Lactate @ 60drops/min). Vaginal examination was performed every 4 hours to assess the progress of labor. Once started, oxytocin infusion was continued to delivery unless otherwise indicated.

Abnormal labour was defined very specifically

1. *Failed induction of labour* as when the patient was not in active phase after 12 hours.
2. *Failure to progress in active phase of labour* was defined as failure of further cervical dilatation

after 4 cm dilatation or of descent of the presenting part after 2 hours of adequate uterine contractions.

3. *Failure to progress in the second stage of labour* 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.

The decision to perform a cesarean delivery was made based on our usual obstetric practice, and the indication for the cesarean section was recorded (failed induction of labour, failure to progress in established labour, or non reassuring fetal status [based on FHR patterns]). At delivery apgar scores were determined. The criteria for diagnosing chorioamnionitis were temperature more than 38 degree Celsius with any two of the five features, viz. maternal tachycardia, fetal tachycardia, uterine tenderness, foul discharge and maternal leukocytosis (WBC> 15,000/cubic mm).

Outcome Measures

Evaluation of efficacy, safety and tolerance of both drugs in group A and B was done by noting following parameters

1. Interval from induction to active phase of labour
2. Interval from induction to delivery
3. Mode of delivery
4. Indications for LSCS
5. Maternal complications
6. Neonatal complications

Statistical Analysis

Statistical Analysis was performed with help of Epi Info (TM) 3.5.3. EPI INFO is a trademark of the Centers for Disease Control and Prevention (CDC).

Group A

In this group, 100 women were induced with intravaginal 0.5 mg dinoprostone gel followed by oxytocin latter. This group formed the test group.

Group B

In this group, 100 women were induced with oxytocin alone. This group was labelled as control group.

The two groups were comparable for age & period of gestation.

Chi-square (χ^2) test showed that there was no significant association between age and groups (p>0.05). The mean age (mean± s.d.) of Group-A was 26.59±3.19 years with range 19-35 years and the median age was 26.0 years. The mean age (mean± s.d.) of Group-B was 25.83±2.91years with range 19-33 years and the median age was 25.5 years. t-test showed that there was no significant difference between the mean age of the two groups (t_{198}=1.76; p>0.05). Thus the patients of the two groups were age matched.

Table 1: Distribution of the patients in the two groups

Group	Number	%
A	100	50.0%
B	100	50.0%
Total	200	100.0%

Table 2: Age distribution of the patients

Age Group (in years)	Group A (n = 100)	Group B (n = 100)	Total
18-23	10	12	22
Row %	45.5	54.5	100.0
Col %	10.0	12.0	11.0
24-29	71	77	148
Row %	48.0	52.0	100.0
Col %	71.0	77.0	74.0
30-35	19	11	30
Row %	63.3	36.7	100.0
Col %	19.0	11.0	15.0
Total	100	100	200
Row %	50.0	50.0	100.0
Col %	100.0	100.0	100.0
Mean ± S.D.	26.59± 3.19	25.83± 2.91	

p=0.27 NS-Not Significant

Table 3: Distribution of patients according to Bishop's score at 0 hour

Bishop's score	Group A (n= 100)	Group B (n= 100)
0-2	63	66
Row %	48.8	51.2
Col %	63.0	66.0
3-5	37	34
Row %	52.1	47.9
Col %	37.0	34.0
Total	100	100
Row %	50.0	50.0
Col %	100.0	100.0
Mean ± S.D.	1.95±1.34	1.86±1.38

t-test showed that there was no significant difference between the mean Bishop's score at 0 hour of the two groups (t_{198}=0.74;p>0.05).

Most of the patients (88%) of Group-A achieved active phase of labor compared to Group-B (76%) which was significantly higher in Group-A ($p<0.05$).The mean interval between induction to active phase (mean±s.d.) of Group A was 8.82±4.32 hours with range 7.9 – 9.6 hours and the median was 8.80. The mean interval between induction to active phase (mean± s.d.) of Group B was 6.73±4.7 hours with range 6.4 – 7.1 hours and the median was 6.70.

Table 4: Distribution of patients according to duration of induction to delivery interval

Interval in hrs	Group A (n = 78)	Group B (n = 61)
12.0 – 13.0	0	46
Row %	0.0	100.0
Col %	0.0	75.4
13.1 – 14.0	73	15
Row %	83.0	17.0
Col %	93.6	24.6
14-1 – 15.0	5	0
Row %	100.0	0.0
Col %	6.4	0.0
total	78	61
Row %	56.1	43.9
Col %	100.0	100.0
Mean ± S.D.	13.70±9.19	12.82±8.27

The mean induction to delivery interval (mean± s.d.) of Group A was 13.70±9.19 hours with range 13.4– 14.10 hours and the median was 13.60 hours. The mean induction to delivery interval (mean± s.d.) of Group B was 12.82±8.27 hours with range 12.4 – 13.41 hours and the median was 12.80. t-test showed that there was no significant difference in mean induction to delivery interval of Group-A and Group-B ($t_{137}=1.53$; $p>0.05$). Proportion of VD in Group-A (78%) was significantly higher than that of Group-B (61%) ($Z=2.20$; $p<0.05$). Proportion of LUCS in Group-A (22%) was significantly lower than that of Group-B (39%) ($Z=3.93$; $p<0.01$). Test of proportion showed that there was significant difference in the proportion of patients with fetal distress in Group-A and Group-B ($Z=1.14$; $p>0.05$). However, proportions of failed induction and Non progress of labour (NPL) were significantly higher in Group-B than that of Group-A ($p<0.01$). In Group-B proportion of women with indication for caesarean section was mainly failed induction and non-progress of labor (87.2%) and only 12.8% had caesarean section for fetal distress. Proportion of non-progress of labour in Group-B was 3 times higher than that in Group-A. Also proportion of failed induction was more than 2 times in Group-B.

The risk of clinical chorioamnionitis was 2.43 times [OR-2.43 (0.61, 9.69); $p=0.19$] more in Group-A in comparison with Group-B but the risk was not significant. Similarly there was no significant difference in both the groups in terms of neonatal jaundice, neonatal sepsis & NICU admissions.

Results and Discussions

Prelabour rupture of membrane has a major impact on fetal and maternal outcome, complicating the pregnancy leading to maternal complications, increased operative interference, neonatal morbidity and in some cases, mortality. There is a general agreement that the term and near term pregnant patients with PROM should be delivered to avoid infection to both mother and the infant as the dangers of infection goes on increasing with prolonged latent period [3]. Cervical condition exerts a significant influence upon induced labour outcome and in consequence the decision about how to induce labour must take into account the favourability of the cervix. More than 12 different pelvic or cervical scoring schemes have been described during the past 70 years, but the semi-quantitative clinical scoring system described by Bishop is the one most widely employed (Bishop 1964). Intravenous oxytocin, available since the 1950s, has been the most commonly used method of induction for women with a viable pregnancy and favourable cervix [4]. It is concluded that cervical ripening with PGE2 gel in patients with PROM and unripe cervix near term significantly improves the outcome for both mother and child [5]. A prospective randomized study was done in 1997 in pregnant women with term PROM to compare the two inducing agents- PGE_2 gel and oxytocin. They found that patient induced with cerviprime gel had better Bishop's score after 6 hours and 12 hours than those patient who were induced by oxytocin and vaginal delivery rate was also high among them. And induction -delivery time was also less in that group. Incidence of puerperal infection and neonatal infection was also lower in cerviprime gel group of patients [6]. Crane JM found that PGE_2 compared with intravenous oxytocin, results in a higher rate of vaginal delivery within 24 hours but it increases maternal infection [7]. In a study done by Vrtacnik-Bokal E PgE2 was found to be effective in labor induction; the rate of caesarean sections was 18.75% in the group induced by PGE2 and 29.41% in the oxytocin

induced group [8]. It is also close to the results of the study conducted by Akhter S et al. which showed out of the 60 patients induced with PGE2, 45 patients (75%) and out of the 60 patients induced with oxytocin 30 patients (50%) delivered vaginally within 24 hours [9].

The present study is undertaken to compare the safety and effectiveness of induction with PGE_2 gel followed by oxytocin and induction with oxytocin alone in term PROM. In total, 200 women were randomized to treatment with oxytocin (n=100) or dinoprostone followed by oxytocin (n =100).Vaginal delivery within 24 hours of labor induction was significantly increased with sustained released dinoprostone followed by oxytocin infusion (78% vs 61%; p = .013).

More cesarean section deliveries were performed in the oxytocin group (39%vs 22%). Failed induction was the most common cesarean indication in the oxytocin group. A significantly higher percentage of patients treated with sustained-released dinoprostone followed by oxytocin infusion achieved active labor (88% vs 76%). The mean active phase duration was shorter in the oxytocin than in the sustained-released dinoprostone– oxytocin group (6.7 vs 8.8 hours). However, it was not statistically significant. Additionally, mean induction-vaginal delivery intervals were similar in both groups (12.8 vs 13.7 hours).

No significant difference in maternal outcome with respect to postpartum hemorrhage (500 mL) or chorioamnionitis was found between the groups. No maternal death or uterine rupture occurred.

Conclusion

The present study showed that use of sustained-released dinoprostone followed by oxytocin for induction of labor in term PROM led to a significantly higher proportion of women with vaginal delivery within 24 hours of induction, and a small proportion of women who required cesarean section compared with the use of oxytocin alone. Induction failure was 2 times more frequent in the oxytocin group (22 cases vs 10 in the sustained-released dinoprostone followed by oxytocin group). This result was not surprising because unfavorable (<6) Bishop's score at admission for induction of labor are associated with a 2- to 3-fold increased risk of cesarean delivery, whereas a score of>5 is usually associated with a probability of vaginal delivery after labor induction, similar to that after spontaneous labor. When the dinoprostone was used for induction of labor, the Bishop score increased in the first 6 hours.Strengths of this study include its design as a large randomized trial. Despite these strengths, there are some limitations. First, the women and caregivers were not blinded to allocation; decisions to intervene might have been susceptible to bias as a result of earlier recourse to cesarean section due to anxiety about experimental therapy in the sustained-release dinoprostone followed 6 hours later by oxytocin group.Despite these limitations, the current study shows that sustained-released dinoprostone followed by oxytocin infusion is an alternative method for the induction of labor, along with oxytocin infusion alone, in term pregnant women with PROM because it has a higher vaginal delivery within 24 hours with no difference in induction–delivery interval or maternal–neonatal complications.

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