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A Comparative Study of Efficacy and Safety of Misoprostol Versus Oxytocin Infusion in Labour Augmentation In Prom

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Abstract

Introduction: *Premature rupture of membranes (PROM) is the spontaneous breach of the chorioamnion with the release of amniotic fluid before the onset of labour.*

PROM occurs in approximately 10% (Gunn et all) of all pregnancies and 60-80% occur in term pregnancy. About a third of these occur prior to 37 weeks and approximately 81% of patients went into labour within 24 hrs and 90% within 72 hrs. Preterm PROM is rupture of membranes before 37 completed weeks. PROM is often associated with significant maternal and perinatal infections.

Prolonged PROM: A case premature rupture of membranes in which more than 24 hours has passed between the rupture and onset of labour

Aims and Objectives: *To compare the safety & efficacy or oral misoprostol with oxytocin infusion in induction of labour in PROM regarding the following:*

- *Latency period(induction –onset of contractions)*
- *Induction –delivery interval*
- *Mode of delivery*
- *Maternal and perinatal outcome*

Methodology: *This study was conducted in the Dept of OBG, Guntur Government Hospital, from april 2017 to may 2018.*

100 patients with PROM, who were not in labour were enrolled in the study & were randomized to one of the 2 management protocols. All recruited patients were counselled & informed consent was obtained. Patients randomized to misoprostol group were given 50µg orally at four hourly intervals as required for a maximum of 6 doses till they got adequate uterine contractions. Patients randomized to oxytocin group were started with 2mIU/min infusion and increased every 15-20 min by 2mIU until there were 3 uterine contractions each lasting 40-45 seconds in 10 min.

Patients who satisfied the following criteria were recruited into the study.

Singleton uncomplicated pregnancy with cephalic presentation, Spontaneous rupture of membranes, Bishop's score 0-5, Primi or multi gravid, Clear liquor per vaginum, No detectable uterine contractions.

Main outcome measures that were studied were:

Induction to delivery interval, Mode of delivery, Maternal complications, Perinatal outcome, Safety and efficacy of misoprostol compared to oxytocin.

Student 't' test & Mann – Whitney test were used for data analysis & P value of<0.05 was considered significant.

Observations and Results: *84% women delivered with 100ug of misoprostol, cost of induction was 10/-. Meconium stained liquor in 2 cases and hyperstimulation was found in one case. Average latency period in misoprostol is 5% vs 7% in oxytocin group. Induction delivery interval is 9.20hrs vs 14.13hrs in oxytocin group. 5 cases from misoprostol group and 6 cases from oxytocin group underwent LSCS (10%vs 12%). No significant difference in the complications of third stage of labour. Maternal outcome like incidence of PPH, caesarean birth, infection, and gastro intestinal side effects and neonatal outcome including APGAR score, infection ,admission into NICU is similar in both the groups. Labour induction with oxytocin infusion for PROM in an unfavourable cervix is associated with longer induction delivery interval. Despite oxytocin resulting longer induction –delivery interval there was no adverse outcome to mother and neonates.*

Conclusion: *Oral misoprostol is easy to administer than titrated intravenous oxytocin administration. misoprostol offers several advantages such as longer shelf life, stability at room temperature and easy administration. It has the advantage of exact dose preparation. It avoids intravenous infusion and continuous monitoring. it is effective even in cases of poor bishops score. It also relieves patient's anxiety and easy mobility. It is an acceptable alternative to traditional oxytocin for labour induction and augmentation in PROM.*

Introduction

Premature rupture of membranes (PROM) is the spontaneous breach of the chorioamnion with the release of amniotic fluid before the onset of labour. PROM occurs in approximately 10% (Gunn et all) of all pregnancies and 60-80% occur in term pregnancy. About a third of these occur prior to 37 weeks and approximately 81% of patients went into labour within 24 hrs and 90% within 72 hrs. Preterm PROM is rupture of membranes before 37 completed weeks. PROM is often associated with significant maternal and perinatal infections.

Prolonged PROM: A case premature rupture of membranes in which more than 24 hours has passed between the rupture and onset of labour

Mid trimester PPROM or pre-viable PPROM: premature rupture of membranes that occur before 24 weeks.

The rationale for advocating active management of PROM with immediate stimulation of labour is that infection may supervene if delivery is delayed14-15. An active approach involving immediate administration of oxytocin to induce labour in patients with an unfavourable cervix has proven to be relatively ineffective, resulting in prolonged inductions. Induction failure is associated with high rate of cesarean delivery. It is postulated that this may be related to an underlying dystocia caused by deficiency in prostaglandin production or in prostanoid biosynthesis.

Misoprostol (CYTOTEC) is inexpensive, synthetic PGE1analogue marketed as oral tablet. It is stable at room temperature & available in 2 formulations, 100 µg & 200µg. A no of controlled trials27-33 show that misoprostol is an effective agent for cervical ripening & labour induction in patients.

The present study was conducted to compare the safety & efficacy of oral misoprostol with oxytocin infusion in induction and augmentation of labour with PROM & in shortening the interval between ROM & delivery.

Aims and Objectives

To compare the safety & efficacy or oral misoprostol with oxytocin infusion in induction of labour in PROM regarding the following:

- Latency period(induction –onset of contractions)
- Induction –delivery interval
- Mode of delivery
- Maternal and perinatal outcome

Materials and Methods

This study was conducted in the Dept of OBG, Guntur Government Hospital, from April 2017 to May 2018.

100 patients with PROM, who were not in labour were enrolled in the study & were randomized to one of the 2 management protocols. All recruited patients were counselled & informed consent was obtained. Patients randomized to misoprostol group were given 50µg orally at four hourly

intervals as required for a maximum of 6 doses till they got adequate uterine contractions. Patients randomized to oxytocin group were started with 2mIU/min infusion and increased every 15-20 min by 2mIU until there were 3 uterine contractions each lasting 40-45 seconds in 10 min.

Patients who satisfied the following criteria were recruited into the study.

1) Singleton uncomplicated pregnancy with cephalic presentation.
2) Spontaneous rupture of membranes.
3) Bishop's score 0-5.
4) Primi or multi gravida.
5) Clear liquor per vaginum.
6) No detectable uterine contractions.

Patients with previous LSCS, PIH, IUGR, multiple pregnancy, diabetes, temp>380C, meconium stained liquor or with any medical diseases like bronchial asthma, cardiac disease or with uterine activity and grand multis were excluded.

Per vaginal examination under aseptic precautions was done to exclude occult cord prolapse & to assess Bishop's score. A bishop's score of 5 or less than 5 indicated an unfavourable cervix.

Bishop Score

Score	Dilatation	Effacement	Station	Cervical consistency	Cervical position
0	Closed	0-30	-3	Firm	Posterior
1	2-Jan	40-50	-2	Medium	Midposition
2	4-Mar	60-70	-1,0	Soft	Anterior
3	5 0r more	>80	+1,+2	-	-

Routine Investigations: Total WBC count & differential counts and Hemoglobin estimation. blood grouping and typing and complete urine examination were done in each patient on admission.

All patients received prophylactic antibiotics (Injection Ampicillin – 500mg after test dose IV 6th hourly).

All patients were monitored by intermittent auscultation. Continuous cardiotocography monitoring was advocated as and when required. A vigilant watch was maintained to detect signs of chorioamnionitis. Labour was monitored in each patient with a partogram. if the cervix was found unripe even after 4 hrs, 50ug of misoprostol was repeated to a maximum of 4 doses till adequate uterine contractions.

II &III stages of labour are managed as usual, following the standard protocols of the hospital. at birth weight and Apgar score of newborn at 1&5 min were recorded. Patients in both the groups were followed up for atleast 7 days.

In the postnatal period, patients were discharged on the 2 nd postnatal day after both normal and outlet forceps delivery. Patients with LSCS, suture removal was done on 7th post operative day and patients were discharged on 8th day.

Main outcome measures that were studied were:

a) Induction to delivery interval
b) Mode of delivery
c) Maternal complications
d) Perinatal outcome
e) Safety and efficacy of misoprostol compared to oxytocin.

Student 't' test & Mann – Whitney test were used for data analysis & P value of<0.05 was considered significant.

Definition and Criteria

1) In misoprostol group, induction was considered failed if there is no change in the Bishop's score 4 hrs after the last dose of PG & no documented uterine activity.
2) In oxytocin group, failed induction was defined as failure to enter active phase of labour within 12hrs after start of oxytocin drip.
3) Tachysystole was defined as more than 5 uterine contractions per 10 min without fetal heart rate (FHR) changes, for 2 consecutive 10 min period.
4) Hyperstimulation was defined as exaggerated uterine response (tachysystole or prolonged uterine contraction of > 90 sec) accompanied by FHR deceleration or tachycardia (fetal heart rate > 180bpm) or reduced variability, late decelerations and variable decelerations.

Observations and Results

1) Age Distribution

Most of the cases selected in study and control group are between 21-25 years of age, but no significance could be attributed to it because most antenatal mothers belong to this age.

2) Gravidity

Most of cases/contols are primigravida, care is taken such that the number of mothers each gravida are nearly equal in both groups to allow better comparison.

3) Gestational Age

Majority of mothers belonging to term gestation. 43 cases of misoprostol, 46 cases of oxytocin group belong to term gestation 7(14%) cases of misoprostol groupand 3(6%) cases of oxytocin group 36 weeks.

4) Bishop Score at Admission

Bishop score	Misoprostol group (n:50)	Oxytocin group (n:50)
0	4(8%)	1(2%)
1	3(6%)	4(8%)
2	6(12%)	4(8%)
3	8(16%)	9(18%)
4	17(34%)	14(28%)
5	12(24%)	18(36%)
Total	50	50

Most of the cases had fallen into scores of 4&5 in both groups.

5) Total Dosage of Misoprostol

Majority of cases delivered with 100ug of misoprostol which accounts for38 cases(76%) and 4 cases(8%) delivered with single dose (50ug) of misoprostol, 5(10%) cases needing 3 doses (150ug), 3 cases requiring 4th dose (200ug). Cost of induction for majority of cases is 20/-.

6) Side effects of Misoprostol

Meconium staining of liquor which is one of the expected complications of induction with PGE1 analogue was seen in 2 cases. Tachysystole was observed in 1cases.

7) Induction to Pain Interval

37 (74%) Cases of misoprostol group have induction pain interval <3hrs and 34(68%) of oxytocin group had an induction to pain interval of<3hrs which is statistically not significant of p value 0.451.

8) Induction - Delivery Interval

Majority of cases in misoprostol group(86%) in the present study delivered within 12 hrs where as majority of cases in oxytocin group(88%) has delivered within 18hrs. The mean induction delivery interval in misoprostol being 9.5 hrs and in oxytocin group it is 14.2 hrs with a statistical significance of($p<0.05$).All cases have delivered within 24 hrs.

9) Prom Delivery Interval

70%of cases in misoprostol group have delivered within 6-12 hrs of prom where as 78% of cases in oxytocin group have delivered within 12-18 hrs of rupture of membranes. this mirrors the findings of induction delivery interval.

10) Mode of Delivery

Mode of delivery	Misoprostol group	Oxytocin group
Spontaneous vaginal	42(84%)	40(80%)
Outlet Forceps	3(6%)	4(8%)
Abdominal	5(10%)	6(12%)
Total	50	50

Table showing spontaneous vaginal delivery in 42 cases of misoprostol group and 40 cases of oxytocin group which accounts for (84%) vs (80%). 3(6%) are delivered by outlet forceps in misoprostol group and 4(8%) had instrumental delivery in oxytocin group. 5cases in misoprostol group and 6 cases in oxytocin group had emergency LSCS for varied reasons. This accounts for P value of 0.451 which is statistically not significant.

11) Indications for Caesarean Delivery

LSCS was done in 3 cases for prolonged labour in oxytocin group but only one case in misoprostol group. There is hyper stimulation in 1 case of misoprostol group for which LSCS was done. There is 1 case of failed induction in oxytocin group and 1 case of fetal distress in both the groups for which LSCS was done. Among sections done for meconium stained liquor 2 cases were from misoprostol group and 1 case from oxytocin group.

12) APGAR score

5 min APGAR score of 0-4 noticed in only 1 case of misoprostol group and oxytocin group. 4 cases of APGAR 5-7 in both the groups at 1 min later improved to an APGAR of 8-10 at 5 min. the

neonatal outcome in both groups are similar of P value <0.5 which is not significant.

13) Admission to NICU

Premature babies in both the groups did well. Meconium aspiration occurred in 1 case of misoprostol group which is delivered by LSCS died after 24hrs.1 baby from oxytocin group died of birth asphyxia and 1 baby from oxytocin group died of neonatal seizures at NICU. perinatal outcome in both the groups were similar

14) Maternal Complications in Postoperative/ Postnatal Period

Observation	Misoprostol group	Oxytocin group
Episiotomy wound infection	0	1
LSCS wound infection	1	0
Maternal mortality	NIL	NIL

The maternal complications are not very significant in both the groups.

Conclusions

In this study cases distributed equally in both groups according to age, parity, gestational age, bishops score at admission to yield better comparative results.

- 84% women delivered with 100 ug of misoprostol, cost of induction was 10/-
- Meconium stained liquor in 2 cases and hyperstimulation was found in one case.
- Average latency period in misoprostol is 5%vs 7%in oxytocin group.
- Induction delivery interval is9.20hrs vs 14.13hrs in oxytocin group.
- 5 cases from misoprostol group and 6 cases from oxytocin group underwent LSCS (10%vs 12%)
- No significant difference in the complications of third stage of labour.
- Maternal outcome like incidence of PPH, caesarean birth, infection, and gastro intestinal side effects and neonatal outcome including APGAR score, infection, admission into NICU is similar in both the groups.
- Labour induction with oxytocin infusion for PROM in an unfavourable cervix is associated with longer induction delivery interval. Despite oxytocin resulting longer induction –delivery interval there was no adverse outcome to mother and neonates.

Oral misoprostol is easy to administer than titrated intravenous oxytocin administration. misoprostol offers several advantages such as longer shelf life, stability at room temperature and easy administration. It has the advantage of exact dose preparation. It avoids intravenous infusion and continuous monitoring. it is effective even in cases of poor bishops score. It also relieves patient's anxiety and easy mobility. It is an acceptable alternative to traditional oxytocin for labour induction and augmentation in PROM.

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